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Virus Pneumonia

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OVER the past decade there has been a remarkable shift in the broad picture of pneumonia on this continent which has reached its culmination in the past five years of chemotherapy. About 1925 a decline in mortality from the disease began and was sharply accelerated between 1930 and 1937. Although attention was being increasingly centered upon specific therapeutic procedures during this period, there is little reason to believe that serum therapy was so widely employed as to account for the observed decline. Nor does it seem that other influences introduced in the development of pneumonia control programs could be credited with the effect. It appears that the decreasing mortality was to a large extent related to natural causes—indicating by this the numerous features in the biological balance which are not known. That this is so is shown by the parallel decrease in mortality from other infectious diseases over the same interval.

In the latter part of the period a number of reports called attention to prevalences of pneumonia, especially in adolescents and young adults, which did not behave like the pneumonias caused by the usual bacterial agents. The last five years have witnessed an increasing consciousness of this picture so that the impression is gained that it now is of greater frequency than the pneumococcal pneumonias. The enhanced incidence has been, interestingly enough, correlated with a number of other events:

Certain of the studies referred to were aided by the Commission on Influenza, Board for the Investigation and Control of Influenza and other Epidemic Diseases in the Army, Preventive Medicine Division, Office of the Surgeon General, United States Army.

Presented at the wartime conference and thirty-second annual meeting of the Canadian Public Health Association, held in Toronto on October 4 and 5, 1943.

1. The rather uniform effort to identify the bacterial agents in cases of pneumonia by pneumococcus typings and cultures of the sputum or blood has created a greater awareness of the need for etiological diagnosis. This has revealed an increasing number of cases in which significant bacterial agents were not encountered.

2. The availability of X-rays in establishments where large groups of individuals are drawn together, schools, industry, military forces, has aided in the recognition of pulmonary involvement in many instances which would not be so interpreted on the basis of physical examination or clinical course.

3. In addition to a decline in the mortality for pneumonia there has apparently been a reduced incidence of pneumonia due to the types of pneumococcus most commonly found in earlier years.

4. The widespread use of chemotherapy and recognition of the prompt response of pneumococcal and streptococcal pneumonia to sulfonamides suggested that processes which did not respond were of different etiology.

5. There has been a growing realization by the medical profession at large of the role of viruses in the causation of respiratory disease.

The contributions of these correlated influences have resulted, therefore, in pointing out the major features of the disease—a wide distribution of a relatively mild pneumonia in which X-ray evidence is out of proportion to physical signs; in which the usual bacterial pathogens are absent from the sputum and sulfonamide therapy has little effect. There are a few additional features which seem common to the picture: The patient does not usually present the pleural pain, bloody sputum, cyanosis and distress of the characteristic lobar pneumonia. The onset is more gradual after a prolonged incubation period; the course is longer and physical signs may not be noted for several days after the onset. Leukocytosis is not a common accompaniment. Practically all cases recover.

This illness has been designated by various terms, the most common ones of which are atypical pneumonia, virus pneumonia, and acute pneumonitis. The ease with which one of these diagnoses can be made has had a great effect in the spread of the disease and while primary atypical pneumonia served a definite purpose in emphasizing the fact that the illness was not typical of usual bacterial pneumonias as well as suggesting that the pulmonary involvement was a primary response, the avidity with which it is now applied to all sorts of respiratory conditions makes pertinent the question, "atypical of what?" Nevertheless, the criteria mentioned and the broad view have tended to some uniformity of concept corresponding to that already stated. In addition, however, certain groups of cases have been reported—such as those of Reimann (1), Kneeland and Smetana (2), Longcope (3)—in which the illness was severe, transmitted in sequence by contact, and the mortality was relatively high. The course of events in these instances differs so clearly from the common one as to indicate that either a different condition was being encountered or that it was a much more virulent form. Considering the common picture more typical, certain inferences can be drawn from the epidemiological evidence.

The incidence is difficult to determine. The Commission of the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the

Army, working at Camp Claiborne, Louisiana, noted an average incidence of 28 per 1,000 per week in the winter months which had been preceded by a rate of 88/1000/week during an "epidemic" period in the summer (4). Reimann (5) estimates that 15 per cent of the cases of pneumonia on his service in 1941 were of this nature and that in 1942 they outnumbered pneumococcus pneumonias by three to one. It seems, however, that the incidence of atypical pneumonia bears a relation to the amount of upper respiratory infection in circulation, and it is of considerable interest to note that there is a tendency for the summer months to constitute the period in which the disease begins to mount.

The mortality is also undetermined. It seems likely that the uncomplicated pneumonia is rarely fatal and that in the past two years a case fatality of 0.1 per cent has not been exceeded.

The contagiousness of the disease must be considered in broad limits. The Claiborne Commission clearly recognized the fact that a definite group of cases which never developed pulmonary lesions presented much the same clinical picture and course as the pneumonic patients. Moreover, still others had a short upper respiratory infection with symptomatology and other features similar to the early days of atypical pneumonia. Reimann and Havens (6) described an epidemic of respiratory disease in a hospital group, only 6 per cent of whom had pneumonia.

There is, apart from certain groups already mentioned, little evidence that the pneumonia, *per se,* is highly contagious. Hospital personnel has been reported to be more commonly affected than other groups but this applies as well to other respiratory disease. One also hears of families involved seriatim. On the other hand, 70 cases in the hospital at one Army post had come from 60 different barracks; in another, 80 cases had come from 69 different barracks. In other words, there is little tendency for the pneumonia to congregate selectively. By and large, the distribution of the pneumonia is so random as of itself to suggest that the pulmonary involvement is not the primary process but rather that it represents an episode in the course of a basic disease determined by factors other than the presence of infection. In this sense it is clear that the underlying illness is readily transmissible and an explanation is offered for the parallelism in curves of upper respiratory disease and atypical pneumonia.

The etiologic concept uppermost in the minds of interested observers is discerned in the phrase "virus pneumonia." It connotes an entity, the causative agent of which is established. A brief review of the situation clearly reveals how far this is from the fact. That pneumonia may occur in the course of virus infections, such as measles, smallpox or psittacosis, is well recognized. That the pneumonias of measles and psittacosis are closely similar etiologically is not, however, the case. Through studies in experimental animals with viruses of vaccinia, psittacosis, and influenza (of both swine and human origin) it became apparent that in the pulmonary lesions produced by these viruses, at least, certain common features existed. The edema of the alveolar walls, the tendency to peribronchial or perivascular cuffs of mononuclear cells and the scanty exudate of large mononuclear cells in edema fluid are common to all. Moreover, epithelial injury is frequently seen. It was natural, therefore, that these viruses

were the first to be considered. It can be definitely stated, however, that psittacosis, ornithosis, influenza A and influenza B can be eliminated as significant contributors to the widespread atypical pneumonia of the past two years (7). The report of Smadel (8) on the identification of 15 cases of psittacosis in 45 instances of atypical pneumonia, while not representative of true conditions, does, nevertheless, continue to emphasize the constant hazard which this disease represents.

It must be borne in mind that cross reactions between the viruses of typical psittacosis, ornithosis, meningo-pneumonitis, lymphogranuloma venereum occur in the complement-fixation test and a positive reaction does not indicate which of the agents may be involved (9). A single positive test may merely reflect an earlier infection by one of these agents, especially in colored individuals. A rise in antibodies in the course of the disease is of much greater significance. The immunological variations among representatives of the group have not been sufficiently well charted as yet to permit rapid differentiation on these grounds alone.

Among the earliest indications of the presence of virus of another nature in cases of atypical pneumonia were those reported by Reimann (1). In that instance studies conducted both by Magill and myself and by Stokes and his associates gave evidence of the transmission to mice of an agent producing low grade meningeal and pulmonary disease. Unfortunately, the effect decreased with passage and finally petered out.

Since that time a number of investigators have made preliminary reports concerning viruses with various characteristics which were encountered in studies of material from cases of atypical pneumonia.

Weir and Horsfall (10) reported in 1940 the establishment of a virus in the mongoose inoculated with sputum or throat washings of patients with acute pneumonitis. They further showed that the convalescent serum of such patients reduced the frequency with which infection took place in comparison with serum from the acute stage of the disease. No confirmation of the work has appeared.

An outbreak of pneumonia occurring among workers at the National Institute of Health in 1940 was shown to have been due to the rickettsial infection, Q fever (11, 12). Studies have shown no relationship of that agent to atypical pneumonia at large.

Eaton, Beck and Pearson reported the recovery of a virus resembling meningo-pneumonitis from human cases of atypical pneumonia (13).

In November, 1942, Baker (14) described a virus recovered from pneumonia in cats which produced pneumonia in mice and normal kittens. The virus formed elementary bodies similar to those of the psittacosis group. He concluded, on the basis of serological studies which were not detailed, that the virus was the same as, or closely related to, the one causing some of the atypical pneumonia in man. Examination of the virus in our laboratory revealed that serologically it was of the psittacosis-L.G.V. family, giving complement fixation reactions which differed in no significant manner from those obtained in studies with other members of the group. Its importance seems to be, therefore, only that it represents another virus of this group found in still another animal species.

In December, 1942, Blake, Howard and Tatlock (15) published a report of atypical pneumonia in four members of a family and 11 of their cats. A virus recovered from the lungs of one of the cats was not transmitted to mice but was pathogenic for kittens, and differed from that described by Baker. The relationship of the cat virus to the human infection was considered suggestive.

At this time Eaton, Meiklejohn, Van Herick and Talbot (16) described the production in cotton rats of pulmonary lesions by a virus-like agent in sputum from cases of atypical pneumonia. Approximately one-third of the specimens of sputum collected from patients in the first nine days of the disease were effective and six strains were adapted by passage. No inclusion bodies were found in involved tissues. Animals immunized by inoculation of human material were resistant to infection with the established strains. No serological relation of the passage material to human disease was demonstrated. This study reveals a greater uniformity in results than those preceding but the possibility of a carrier virus in cotton rats has not been completely eliminated.

Horsfall and his associates (17) later reported the fact that sputum or throat washings from atypical pneumonia induced in cotton rats the formation of antibodies to a strain of mouse pneumonia virus. Moreover, the serum of inoculated animals and of certain convalescent patients reduced the frequency with which sputum would produce lesions in cotton rats. Returning to the study of earlier mongoose material, similar serological effects were obtained. Thus, from quite indirect procedures the suggestion was made that the inhibiting action of the sera tested represented antibodies to a virus in the sputum of patients which is antigenically related to the virus established in the mongoose or to the pneumonia virus of mice. That the agent was transmissible in series in fertile chicken eggs was indicated also by the development of similar antibodies in animals inoculated with such material. If any of the material was heated before inoculation of animals, antibodies did not arise. This complex system and approach is of considerable interest but its significance is scarcely established.

More recently Rose and Molloy (18) have described the production of pulmonary involvement by the intranasal inoculation of sputum of patients into newly weaned guinea pigs and maintained by passage. The agent was filterable through a Berkefeld filter and was transmissible to cotton rats, although it was not possible to institute the infection in cotton rats with material direct from human subjects. Serological data were again unable to support the relation of the virus to the human disease.

There is thus a wide variety of indications which may in time be resolved into a picture. At the moment, however, it is evident that *a* virus responsible for a large percentage of the cases of so-called virus pneumonia has not been satisfactorily established. It is generally accepted that a single agent will not account for all the cases at present included in this category. Atypical pneumonia has been encountered in outbreaks of upper respiratory disease of sufficiently different pattern as to indicate that they were of different etiologies. Nevertheless, it is my impression that when a high incidence of respiratory infection occurs in a group and the cases present, upon careful investigation, a great uniformity in symptomatology and course, the probability is that the dis-

ease is in large part due to a single species of infectious agent. When atypical pneumonia is encountered under these conditions, it seems likely that a common agent will be involved in the primary infection.

This leads to the suggestion that the causative agent may be more profitably sought in the parent disease rather than in the pneumonic case which would, in this sense, represent an incidental finding. Such appears to be the case in influenza of current years. The factors which determine whether pneumonia is to occur may be more closely related to physiologic phenomena than to the fact that an infection has taken place.

One is tempted to speculate whether the picture seen in atypical pneumonia might represent the underlying process of most bacterial pneumonia and whether the reason it has become more noticeable is related to a relative scarcity of the usual pulmonary pathogens. In their presence, the picture would be modified to conform to that characterizing the pneumonia the particular organism excites. There is at present, however, little information from human sources with which to debate the question.

In this brief review an effort has been made only to indicate the problem of atypical pneumonia in the present state of knowledge and to raise for consideration certain questions as to the significance of the pneumonic process as a primary feature of the diseases with which it may be associated. It seems quite certain that a clinical and X-ray picture of the same type is encountered under a variety of conditions—influenza, measles, and others as yet unidentified. It is obvious that the term "virus pneumonia" must be used with reservations and should in fact be more properly replaced by a nomenclature which does not give such confidence that a single etiologic entity is being encountered. The lack of conclusive evidence in the studies so far reported indicates the difficult nature of the problem. While the search goes on, it seems advisable not to forget that bacterial pneumonias still exist and may increase or that bacteria not ordinarily considered pathogenic may be encountered. Measures for their detection should still be employed.

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Administration of a Provincial Venereal-Disease Control Program

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THE purpose of this conference, as outlined by the Chief of the Division of Venereal Disease Control of the Department of Pensions and National Health, is to consider how existing facilities for the prevention of venereal disease may best be utilized in Canada, and what is needed in the way of modification and extension of these facilities. Accordingly, we are presenting a summary of measures adopted by our Division of Venereal Disease that, in our opinion, constitute a fairly adequate provincial venereal-disease control program. Since our Division is only in its second year of active operation, we shall conclude by suggesting certain modifications or extensions of these facilities which we believe may be needed to improve the program.

In setting up a program for venereal-disease control, we had in mind syphilis and gonorrhoea. Our attention, however, was focused mainly upon syphilis because of the more serious consequences of this disease, because it can be transmitted at birth, and because we lacked weapons to combat gonorrhoea similar to those with which we can detect and cure syphilis—the blood test and the arsenicals. Fortunately, the use of sulfa drugs and the promise of penicillin have changed the therapeutic outlook for gonorrhoea, and the program developed for syphilis applies equally to the control of gonorrhoea.

As a first measure, the Legislative Assembly of Quebec, at the request of the Honourable the Minister of Health and Social Welfare, passed a law for the control of venereal disease which was sanctioned on March 20, 1941, making it compulsory for physicians to declare their venereal-disease cases and for infectious patients to submit to treatment.

Reporting of Cases

The willingness of physicians to declare their venereal-disease cases depends on their interest in our program; and we must strive to stimulate this interest and obtain better reporting through the use of various methods:

1. Supplying free drugs for the treatment of only those cases which have been reported, and limiting the quantity of arsenic and bismuth to three months' treatment.

Presented at the National Venereal-Disease Control Conference, held in Ottawa, December 6-10, 1943.

2. Checking the positive blood tests in the records of our laboratory against the reports of syphilis received by the Venereal Disease Division. At the end of a month the physician is requested by letter to disclose the name of the patient whose serum has been found positive. This control is greatly facilitated by the centralization of the sero-diagnostic work in our provincial laboratory where, in 1942, of 216,000 samples of blood received, more than 17,000 were found positive.

We have made it our duty to assist private physicians in solving their difficulties in the interpretation of diagnostic tests or in treatment. Addresses to medical societies and consultation by correspondence between practitioners and the director of the Division may be considered a third method and the most important one for obtaining not only reports of venereal-disease cases but also the co-operation of physicians in detecting sources of infection and in applying the best therapeutic methods.

Case Finding

The first and most obvious step in syphilis case-finding is the requirement of a routine blood test of every patient applying to a hospital or to a practitioner for medical care. We believe that this practice is followed at present in all the hospitals, clinics and larger obstetrical wards of the Province of Quebec. The blood tests, made freely available to all physicians by the Ministry, have rightly won their confidence, as is evident from the steadily increasing number of these tests, performed in our laboratory; they will reach the 325,000 mark this year. Industries are also giving more and more attention to serologic surveys of their workers.

The reliability of serologic tests is no less important than their general use, and our laboratory has set a high standard of sensitivity and specificity for its serodiagnostic work, using the Kahn diagnostic test together with a special modification of the Wassermann complement fixation method. Concentration of the tests at the Provincial laboratory in Montreal has favoured the maintenance of our standard, whatever the number of specimens received, as 70 per cent are readily eliminated as negative by an ultra-sensitive and rapid screen test.

Adequate laboratory service for dark-field examination of chancre fluids collected and shipped by the capillary-tube method, and examination of smears for the presence of the gonococcus are also available to all physicians. We hope that culturing of gonococci will soon be added as a routine procedure for detecting gonorrhoea.

The medical profession must be trained in the techniques of diagnosis and be persuaded to be on the lookout for syphilis and gonorrhoea regardless of the social and economic status of their patients.

Epidemiologic Approach

By applying to syphilis and gonorrhoea the epidemiologic investigation of contacts and sources of infection, we have made, during the past two years, definite progress in finding infectious cases of these diseases. Only by the use of this method can we detect the ignorant, careless or vicious person who, though infected, does not want medical advice and often escapes routine serologic

testing. Contact tracing makes it possible to find the infection in its early stages and is particularly effective in detecting cases of gonorrhoea.

An experienced health officer, well trained in the epidemiology of venereal diseases, is in charge of this work, which is carried on by twenty-eight specially trained nurses and medical-social workers. Twenty are permanently attached to the large clinics of Montreal, Quebec, Three Rivers and Sherbrooke, for contact tracing and follow-up of treated patients. It is also their duty to make all the investigations required by the Division of Venereal Disease in their own districts. In Montreal, one medical-social worker gives her services to the Juvenile Court, and one to the war industries.

Nurses of the county health units are part-time medical-social workers in the clinics of the small centres. The contact tracing and follow-up in these centres, in centres where no clinic exists, and in the rural districts, are carried on by the staffs of the fifty-six health units. The health officers in charge of these units have all followed specially organized three-week courses in syphilis, gonorrhoea and their control. One of these health officers and a social worker are at present following special courses at Johns Hopkins University and will later become epidemiologists in the Division.

Federal grants to our Venereal-Disease Division have made possible the rapid expansion of our epidemiologic service during the last four months.

Treatment of Patients

The provision of adequate medical service is of prime importance in a venereal-disease control program.

By free distribution of anti-syphilitic drugs to physicians, we not only have stimulated their interest in treatment but we have also assisted in lowering its cost to patients. An increasing number of syphilitic and gonorrhoeal cases are being treated by private physicians, to whom medical abstracts on accepted therapeutic methods are distributed regularly.

For the treatment of indigents suffering from syphilis or gonorrhoea, eighteen clinics receive special grants from the Ministry of Health and Social Welfare. Of these, nine are in Montreal, two in Quebec, seven in smaller centres; and it is hoped that, before long, more small centres will have free clinics.

In those districts where there are no clinics, the treatment of indigents is entrusted to the local physicians who receive, from the Ministry, remuneration for each injection of arsenic and bismuth given.

Some of our clinics, under the direction of the teaching staffs of Montreal, McGill and Laval Universities, are instruction centres for students, for practitioners and for the health officers of our county health units. These, in turn, will teach the practitioners of their counties the methods for controlling venereal diseases.

Law Enforcement

This applies to all patients suffering from gonorrhoea, or syphilis in its contagious stage, who wilfully abstain from treatment. The Director is legally authorized to sign orders for their apprehension and isolation. Prostitutes and

vagrants found infected are isolated while in jail and given treatments of ten weeks for syphilis and two weeks for gonorrhoea.

Education

Posters and pamphlets have been published in both languages and distributed by the thousands to clinics, social agencies, war plants and camps. Sound films have been used to illustrate several lectures. Radio-Canada is generously co-operating with our Division, broadcasting lectures by specialists, spot announcements, and a series of sketches.

The medical profession has profited from meetings and lectures in all parts of the province, and from the frequent distribution of scientific articles on venereal diseases.

Recommendations

We believe that the very rapid expansion of our Division and the good results obtained in such a short time are due, in large part, to the centralization of reporting of cases and of laboratory facilities, as well as of all instructions concerning the epidemiologic and medical-social work. This procedure, in our opinion, should be adopted whenever possible. The co-operation of our health units with our Venereal-Disease Division has been of inestimable value and a principal factor in this rapid expansion.

We should further recommend:

1. That, by effective tracing of contacts of recent venereal-disease infections, evidence of the activities of prostitutes be collected; and that instruction regarding the proper action to be taken with respect to these sources of infection be given by the Venereal-Disease Division to the law-enforcing agencies.
2. That, although law enforcement is a necessary feature of an adequate venereal-disease control program, our main and constant effort should be directed towards educating the public, the medical profession, and others concerned.
3. That the law-enforcing agencies extend to the Division of Venereal Disease all the co-operation and assistance required.
4. That specific laws be enforced against those who participate in or exploit prostitution; that appropriate action be instituted to remove those conditions which facilitate association of prostitutes and healthy persons; and that proceedings against prostitution be taken by federal police, when necessary.
5. That serious thought be given to the possible rehabilitation of prostitutes. Probably a large number could be rehabilitated.
6. That a large share of the instruction given by universities be devoted to venereal diseases and their epidemiological aspects.
7. That blood testing be made compulsory for persons contemplating marriage and for pregnant women.
8. That the Federal Division of Venereal Disease Control in the Department of Pensions and National Health be maintained permanently in order to assist the Provinces in their various problems of venereal-disease control as well as financially.

Health Insurance from the Public-Health Standpoint

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DURING the past session of the Federal Parliament a special committee of the House of Commons gave intensive study to the question of social security, particularly to that phase of social security having to do with national health. The two measures studied were: (1) An Act [the short title of which is the Health Act] respecting Health Insurance, Public Health, the Conservation of Health, the Prevention of Disease, and Other Matters Related Thereto, and (2) The Physical Fitness Bill. These are commonly known as the health insurance bills. The objects of the draft health bill are: (1) to place within the grasp of the people of Canada the benefits of a comprehensive scheme of health insurance designed and organized for the prevention and cure of disease and the conservation of health; and (2) to assist Provinces in strengthening and enlarging their activities in public health and preventive work and services.

I think it is generally admitted that the besetting problem in Canada today—the one that has brought health insurance into consideration—is that in some large areas the people are almost, if not completely, without medical attention and hospital care. (This condition, acute even in pre-war days, is greatly aggravated by the fact that the armed services have taken over 3,000 doctors out of civilian practice and services.) The problem presses for solution. Can it be met by national health insurance or state medicine, by direct action from the Dominion, or aid from the Dominion to the Provinces on a plan definitely laid down by the Dominion? It is the contention of the Government that national health insurance, with its preventive, curative and conservation features, will meet this situation.

The Atlantic Charter and the Beveridge Report have given a stimulus to public thinking on the subject of social security, not only in Canada, but throughout the world.

The Atlantic Charter, issued by President Roosevelt and Prime Minister Churchill on August 14, 1941, places the objective of social security before the United Nations as one of the purposes for which we are fighting the war. It says in paragraph 5: "They [Great Britain and the United States] desire to bring about the fullest collaboration between all nations in the economic field with the object of securing for *ALL*, improved labour standards, economic advancement and *social security*."

This objective has been subscribed to by the Dominion of Canada on more than one occasion, but particularly on January 1, 1942, at Washington, when

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a representative of the Canadian Government formally subscribed on behalf of Canada to the principles embodied in the joint declaration known as the Atlantic Charter. As has been evidenced by party platforms since adopted, there has been no division of opinion between political parties with reference to subscribing to this declaration.

The Beveridge Report, which has to do with social security in the United Kingdom, has had a profound effect upon the world's thinking. It is the work of a most enlightened and progressive authority on social science. While its motives and its reasonings are applicable to humanity everywhere, its specific recommendations are not, in all respects, applicable to Canada. Canada enjoys a relatively large measure of social-security legislation. We have six major social-security measures in operation: workmen's compensation, mothers' allowance, unemployment insurance, old-age pensions, pensions for the blind, and vocational training. Unquestionably the greatest present lack in Canada's system of social security is insurance against the fear of the heavy economic burdens of sickness and ill-health. The most conspicuous gap is in the field of health, and we propose to fill this by the introduction of health insurance.

The Atlantic Charter has as one of its objectives the attainment of freedom from fear. Emotions of all kinds are determining factors in people's health; people are elated and exhilarated when they have a sense of security, but they feel depressed and downcast when an emotion such as fear overtakes them. And while perhaps the framers of the Charter had in mind freedom from fear of violence, freedom from fear of illness—with all its dire consequences—might well have been included. What greater fear haunts humanity than "where through sickness and invalidity, the capacity to earn is gone" or "where the privation consequent upon unavoidable loss of work is aggravated by the necessity of extra outlays?" Those are the fears which can be allayed by a measure of health insurance coupled with the provision of health services for all.

What is health insurance? I conceive it to be a plan whereby payments by or on behalf of a reasonably homogeneous group are made into a common fund, and the benefits of such payments are distributed to those members, and to no others, on certain definite conditions. The patient will receive cash benefits with which he may buy medical services, or benefits in kind in the form of free medical services.

Insurance against the emergency of ill-health is not a new conception. Historically, it appears that the pioneer in the field was Bismarck of Germany who launched a scheme of health insurance in the German Empire as early as 1883. In all, forty-one countries have adopted health-insurance legislation of various types. Of these, thirty-three are compulsory, eight voluntary. These are pre-war figures as far as European countries are concerned, but within the past year or two, compulsory health-insurance schemes have been adopted in four American countries, namely, Argentina, Brazil, Columbia and Mexico. The most complete and comprehensive plan is in Russia, where completely socialized medicine and free treatment are provided for all its people.

In 1911, Lloyd George introduced health insurance in England. At that time

all that was provided for the wage-earner (it was only the wage-earners who were cared for under health insurance in all European systems up to that time) was the visit of the doctor, drugs and a cash benefit. The idea was very largely economical; it was politico-economical from the start. It has been demonstrated that there has been no improvement in the health of the British people through health insurance since it was introduced in England and put into effect in the year 1912. In the first year, 60 per cent of the insured people called the doctor—and 60 per cent of the people still do so. Later it became obvious that *medical care alone was not the best method of handling the problem of health* as far as it affected the people of the various countries of Europe, and some of them began to give consideration not only to the working man but also to his dependents.

In 1920 Sir Arthur Newsholme came out to the United States and under the auspices of the Milbank Memorial Fund he enunciated the idea that public health and preventive medicine should play a primary part in *health insurance* and used the now-common phrase "positive health" for the first time. He had the right idea, and countries which have since adopted health insurance have endeavoured to integrate *preventive medicine* with *medical care*. There is no point in introducing a system of medical care unless it be integrated with preventive medicine. There is no use going on paying out sums of money year after year for the treatment of diseases that are controllable by public-health measures. One of the most recently adopted public-health plans has been that of Chile. Chile has adopted ideas radically different from those that were in existence in Europe. The authorities said: "We must do something for the health of the people of this country, not merely provide them with doctors, nurses and hospitals." The first step was a medical examination of all the people. Since health insurance was introduced in Chile—and it is not complete as yet—600,000 people have been given blood tests and have been X-rayed for tuberculosis. All those who have been found to be suffering from syphilis and tuberculosis have been given free treatment. That gives you an idea of the modern trend, and it is something of that nature that we have had in mind in Canada in preparing and planning health insurance.

There is an infinite variety of schemes—some compulsory, some voluntary, some contributory, others financed entirely by the State. Some insure only the head of the family, others provide in a greater or lesser degree for dependents.

The history of the approach to the subject of health insurance by legislative bodies in Canada is well known and need not be repeated here. British Columbia and Alberta have enacted measures but they have not been put into operation. In 1934, Saskatchewan set up a Health Service Board under whose auspices a number of progressive health measures, including free institutional treatment for tuberculosis, have been adopted. There was a pronounced stirring of interest in the Federal field in 1928 which ended in a recommendation that the Department of Pensions and National Health institute a comprehensive survey of the field of public health with special reference to a national health program.

In 1935, the Bennett Government enacted the Unemployment and Social

Insurance Act, and authorized an administrative commission to assemble information concerning a plan for providing sickness benefits on a co-operative or collection basis, whether by insurance or not. The unemployment-insurance feature was declared unconstitutional by the Privy Council and it is fairly clear that it was the Government's intention that if the unemployment-insurance measure passed the constitutional test in the courts, and its operation proved a success, the Dominion would in due course move into the field of health insurance.

The present proposals have long been under study and in course of preparation. Indeed, since 1928 the health officers of the Department of Pensions and National Health have made it their business to conduct a more or less continuous study of health insurance. A little over a year ago, departmental studies reached a point where it was considered advisable to reduce their information to some definite formula for practical consideration. Accordingly, on February 5, 1942, the Government authorized the formation of an Advisory Committee on Health Insurance.

After consultation with the Provincial Ministers of Health and representatives of professional and lay organizations which included the medical, dental and hospital associations, as well as labour, agriculture and other professional and business groups, the committee brought in certain definite conclusions which are reflected in its proposals. The members laid down six principles underlying the plan, the most important one relating to public health being that "no scheme of health insurance can be successful without a comprehensive health program of a preventive nature."

Dealing with this principle, there are three reasons why health insurance is advocated: (1) the human impulse to relieve and minimize human suffering, (2) the national economic need of a healthy population—or, to express it in a negative way, the national need to eliminate the economic waste arising from ill-health; and (3) the social motive: the desire to relieve the people of the crushing burden of sickness in the home.

If proof were needed for the introduction of a wide measure of preventive features in the health insurance bill, let me recall some of the deficiences now present in the public-health field. Let us take the matter of maternal mortality. A study of the population shows that we are not making progress in Canada. There is a falling birth rate. We have no immigration. The young people are leaving the country in fairly large numbers and we note that, instead of the progressive increase that we had over a very long period of years, we now have what is becoming a decrease; whereas the increase was relatively 20 per cent from 1911 to 1921, it is now only 10 per cent. Maternal mortality is an extremely important factor in respect to population. We have been losing an average of a thousand mothers each year. The rate has fallen a little during the past two or three years, due to the concentrated efforts of Provincial Departments of Health. When a mother dies, the child usually dies. We lack incubators and nursing care. Over the past ten years we have been losing an average of 15,000 children under one year of age. In addition, we are losing 16,000 people a year through

communicable diseases. Why should there be this enormous death rate? The answer is: poverty on the part of parents, who cannot afford to call in a doctor or a nurse or delay calling them until it is too late. Whooping cough and scarlet fever take a large toll, and many adults are lost from influenza, pneumonia and other diseases.

There are two physical conditions that should give us a great deal of concern. One is tuberculosis and the other is mental illness. The incidence of tuberculosis rose sharply in 1941 as a result of large numbers of young people entering industry. Many of them, undernourished and without proper housing, have developed tuberculosis. Since the beginning of the war, tuberculosis has stepped up from eighth place to seventh as a cause of death. We have a definite increase in the number of deaths attributable to tuberculosis directly on account of the war. The situation varies in different parts of Canada. Take Ontario and Quebec, adjoining provinces: in Ontario the tuberculosis death rate is 25 per 100,000, and in Quebec 80. Ontario has provided practically free treatment and is now X-raying the people of the province at a cost of thirty cents per X-ray. In Saskatchewan, where free treatment is also provided, the death rate is 29. In New Brunswick and Quebec, where living conditions are the poorest, the tuberculosis death rate is highest. Malnutrition and bad housing are factors having to do with this condition. What has been done in Ontario and Saskatchewan can be done in other provinces, and we know that, given an opportunity, we can eliminate tuberculosis in one generation.

The situation in regard to mental illness in Canada is also grave. Today there are 47,000 persons in our mental institutions. We are short about 10,000 beds. There are many mentally ill persons for whom no accommodation is available in mental institutions, whereas there are numbers of mentally ill young patients in these institutions who could be out in the world, earning a living, provided the work was of a routine character and devoid of worry, anxiety and competition. In addition, there is the lack of professional and nursing staff, making individual supervision and care for the patients impossible. The prevention of much mental illness is possible through the establishment of psychiatric clinics for the early detection and treatment of mental conditions. Provincial funds are inadequate to meet the requirements for betterment, and the proposal in health insurance will help to meet the needs.

The venereal-disease problem has, at all times, been an extremely serious one. The only way in which the venereal diseases can be adequately controlled is by a complete program including education of the public, the early detection of cases, and free treatment. Such a program would, over a period of years, effect a saving in institutional and hospital cases, in mothers' allowance, old-age pensions and poor relief. Such a program requires additional funds, and these will be supplied under the health-insurance scheme.

Considerable thought is being given today to the prevention and control of the diseases of middle life, such as cancer, heart disease, arterial disease, diabetes, and diseases of the kidneys. Through the adoption of health insurance and through the periodic medical examination of children and adults, much

could be done to prevent the occurrence of these diseases and to extend the life expectancy of persons of middle age.

There is abundant statistical and practical evidence to prove that preventive measures actually reduce the amount of sickness. The use of toxoid in the cities of Ontario had almost completely stamped out diphtheria before the war. The extension of free institutional treatment for tuberculosis has greatly lowered the incidence of that disease. Vaccination has almost entirely eliminated smallpox. Typhoid fever has become extinct due to proper treatment of municipal water supplies and pasteurization of milk. "Safety-first" policies have reduced the accidents in industry. It is not necessary to multiply illustrations. These simple and well-known facts demonstrate that well-conceived preventive measures are capable of reducing the incidence of sickness.

In addition to the main health-insurance grant and the public-health grant for the provision of general health services, it is proposed that the Dominion Government should make direct grants to the provinces for six additional types of preventive measures:

1. The provision of free treatment for all persons suffering from tuberculosis, including the construction of additional buildings and bed accommodation.
2. The provision of free treatment for persons suffering from mental illness and for the care of mental defectives, including buildings and accommodation.
3. The provision of preventive and free treatment for persons suffering from venereal diseases.
4. The provision of training facilities in public-health work for physicians, engineers, nurses, and sanitary inspectors.
5. The undertaking of special investigations concerning public health or public-health measures.
6. The establishing and undertaking of a physical-fitness program for youth.

The need for any particular measure would have to be approved by the Dominion, and the arrangements for carrying out such measures would have to be subject to Dominion approval.

These six schemes are optional but, in order to obtain assistance towards health insurance, the province must qualify for what is called the public-health grant by maintaining health services covering some twenty-four subjects. These are: Standard preventive measures for the prevention and treatment of communicable disease; the provision of expert advisory services; the adoption of a program of public-health education through local voluntary agencies; a mental-hygiene program; the establishment of control services with respect to communicable diseases; the sanitary supervision of premises; the establishment of nutritional services; the maintenance of public-health laboratories; the establishment of sanitary-engineering services; the collection and dissemination of vital statistics; the supervision of hospitals and sanatoria; the provision of dental inspection for children; the adoption of child and maternal hygiene services; the supervision of sanitation and health environment in industry; quarantine inspection to prevent the introduction of communicable diseases into the pro-

vince; the provision of public health nursing services; the adoption of health regulations with regard to housing; an adequate venereal-disease control program; a program for the prevention, detection and treatment of tuberculosis; cancer clinics; preventive and diagnostic services for the early detection of heart disease in children; medical inspection in the schools; investigations of epidemics; and research services. All of these services exist in greater or lesser degree in some of the provinces, but not all can be said to exist in all the provinces.

From what I have said, it will be seen that health insurance from the public-health standpoint is a comprehensive and far-reaching scheme. It is proposed to bring the general practitioner into the preventive field. He is to be the medical adviser. We want him to be responsible for the family when the members are apparently well, and to be the pivot in curative and preventive medicine. If and when health insurance becomes operative, public health will have received a most encouraging stimulus and we will have a basic federal policy in public health—a policy based upon co-operation with the provinces.

The program is fundamental. It marks an epoch in public-health history. It will be clear from this brief review that apart from the reduction of morbidity and mortality of disease the fundamental and primary object is the integration of public health and medical care for the purpose of raising and maintaining the standard of health of the people of Canada.

A Nutrition Survey in East York Township

II. The Influence of the Choice of Dietary Standards upon Interpretation of Data

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THIS survey was concerned with nutritional examination of 546 students in the Collegiate Institute of East York Township (a suburb of Toronto with urban characteristics). In the first report of this series (1) a general statement of the results was given. From records of one week's food intake for each person, calculations were made for the amounts of calories, protein, calcium, iron and four vitamins. These amounts were then expressed as percentages of the recommended allowances approved by the Food and Nutrition Board of the U.S. National Research Council, as adopted for use in Canada by the Canadian Council on Nutrition (2). From the various percentages an average "diet score" was calculated for each person. The value of this diet score was indicated as questionable in the first report but some method of giving a composite rating for food intake is necessary and the one adopted is no more open to question than others which have been used.

One would expect correlation between the pictures of the food intake and the results of physical examinations, especially if one has in mind the extensive claims which have been made regarding the effects of nutrition upon physique and health. While there was an indication of some correlation between the composite dietary ratings and nutritional status as determined by examining physicians, marked discrepancies were evident. The table in which these two sets of data were combined (Table VI in the first report) gave an impression that the grading of food intake was too high. An examination of individual items of the calculated nutrients is useful. On the basis of the standards used, the supplies of calories, protein, iron and vitamin A appeared to be satisfactory, those of calcium and riboflavin fair, but the amounts of thiamin and of ascorbic acid were low. No evidence of deficiencies of either of these vitamins was seen in the persons examined. In commenting on these results in the first report the following statement was made: "Various conclusions may be drawn, any or all of which may prove to be correct: (1) the dietary records did not give a reliable assessment of nutritional conditions, (2) the standards in current use are too high in several respects, or (3) methods of appraisal used in this study were not sufficiently sensitive. The general level of health found in these students was such as to give particular emphasis to the second explanation; reconsideration of nutritional standards is urgently needed." The value of a record of food intake for one week is under investigation in this laboratory at present and the results will be available shortly. Further information on the third explanation is not now available. More detailed examination of the second explanation has been made and the results are presented herewith.

In an appraisal of the influence of dietary standards our attention has been given to two nutrients, thiamin and ascorbic acid. The reason for this limitation is obvious: 56 per cent of the girls and 70 per cent of the boys received less than 70 per cent of the recommended allowances of thiamin. The intakes of ascorbic acid were even less satisfactory, in terms of recommended allowances. These two nutrients were assessed as markedly deficient. This interpretation rested entirely upon the standards; no evidence of deficiency was revealed by physical examination and the health of the students was such as to indicate that no marked dietary deficiencies were present.

Thiamin

The recommended allowances for thiamin were calculated basically, but not consistently, for different age groups, upon the value of 0.6 mg. per 1000 calories. This value was apparently derived from a study on human subjects by Williams *et al.* (3). A recent report by Keys, Henschel, Mickelsen and Brozek (4) states that intakes of thiamin in excess of 0.23 mg. per 1000 calories were no more beneficial, as judged by health and work performance in humans, than the minimal amount (0.23 mg.). The great discrepancy between the two values may be due to differences in fat intake in the two experiments. Subjects in the first experiment received a diet in which fat supplied 26 per cent of the total calories; in the second case, fat furnished 36 per cent of the calories. The sparing effect of fat upon thiamin requirements has been amply proven for rats and was assumed for humans by Williams and Spies. Food intakes recorded in Toronto show fat supplies of 40-45 per cent of the total calories. A possible relation between the amount of dietary fat and thiamin requirement was apparently not considered in determining the recommended allowances. An examination has been made of most of the data available regarding thiamin requirements; whenever possible these have been calculated in the way customarily used of milligrams of thiamin per 1000 calories and, when sufficient information was given, the fat content of the diet has been calculated. All experimentally determined thiamin requirements for various species of animals and for humans are above a base line which has the following values:

No fat in diet, 0.19 mg. thiamin per 1000 calories.
5 per cent calories from fat, 0.18 mg. thiamin per 1000 calories.
41 per cent calories from fat, 0.11 mg. thiamin per 1000 calories.
78 per cent calories from fat, 0.04 mg. thiamin per 1000 calories.

Similar calculations made for diets which caused extensive beri beri in humans, as listed by Williams and Spies (5), give thiamin contents which are all below the base-line. It might be assumed that the base-line indicates minimal thiamin requirements. The lowest value listed by Keys *et al.* is, as far as their results are concerned, an optimal amount for humans. It was obtained with the use of a diet which in fat composition is not far removed from actual food intakes observed in Toronto and it is practically double the base-line value which is apparently minimal. For purposes of recalculation we have taken this amount, 0.23 mg. per 1000 calories, as being the optimal human requirement and have

reassessed the thiamin intakes as percentages of this amount. The original and the present assessments of thiamin supplies are given in Table I. As in the first report, 90 per cent or more of the standard is rated as excellent, 80-90 per cent good, 70-80 per cent fair, and below 70 per cent poor.

TABLE I

COMPARISON OF ASSESSMENTS OF THIAMIN INTAKES
(Figures given are percentages of total number of each sex)

Group	Standard	Grading of Thiamin Intakes			
		Excellent	Good	Fair	Poor
Girls	N. R. C.	12.6	12.2	19.2	56.0
	Keys' estimate	97.2	1.0	0.7	1.0
Boys	N. R. C.	8.5	6.2	15.0	70.4
	Keys' estimate	90.4	5.0	2.7	1.9

The marked difference between the two gradings is, of course, obvious. In the first report in this series it was stated that careful physical examinations showed that 78 per cent of the girls and 85 per cent of the boys had excellent or good health. The new grading of thiamin supplies is much more consistent with the results of physical examination than were the original gradings.

ASCORBIC ACID

As in the case of thiamin the possibility has been considered that the recommended allowances for ascorbic acid are somewhat too large. The Health Organization of the League of Nations recommended a supply of 30 mg. per day; this is markedly lower than the U.S. National Research Council allowances. It is our understanding that the League of Nations' estimate has been widely accepted in Great Britain, that the general population has had supplies based on this estimate during the war, and that deleterious effects have not been noted. The intakes recorded in the East York survey have been reassessed in terms of this allowance, using the same procedure as followed for thiamin. The values for the original assessment and for the new one are given in Table II.

TABLE II

COMPARISON OF ASSESSMENTS OF ASCORBIC ACID INTAKES
(Figures given are percentages of total number of each sex)

Group	Standard	Grading of Ascorbic Acid Intakes			
		Excellent	Good	Fair	Poor
Girls	N. R. C.	8.7	5.9	10.5	74.8
	League of Nations	80.8	4.5	3.8	10.8
Boys	N. R. C.	7.7	6.5	5.4	80.4
	League of Nations	85.4	2.3	3.1	9.2

The comments made regarding the comparison of gradings of thiamin supplies are also appropriate in the case of ascorbic acid. The regrading of ascorbic acid intakes is consistent with the results of physical examinations; the original gradings appeared to be definitely inconsistent.

Composite Diet Picture

Using the original gradings for calories, protein, calcium, iron, vitamin A and riboflavin and the regradings for thiamin and ascorbic acid, the diet scores have been recalculated. Changes from the original calculations would be expected. Average diet scores, original and recalculated, are shown in Table III.

TABLE III

Comparison of Diet Scores
(Figures given are percentages of total number of each sex)

Group	Basis of Grading	Average Diet Scores			
		Excellent	Good	Fair	Poor
Girls	Original	16.1	55.4	22.1	6.6
	Revised	54.2	35.7	8.4	1.7
Boys	Original	11.2	60.5	25.9	3.1
	Revised	54.6	37.7	6.5	1.2

The upward shift in the diet scores, produced by the revaluation of thiamin and ascorbic acid supplies, is clearly evident. The question at once arises as to which of these pictures of food supplies is a more accurate portrayal of nutritional conditions among these students, or, indeed, if either is useful. The nutritional status of each student was assessed by the examining physicians and, while the presence of a large subjective error must be recognized, these assessments form practically the only useful physical evaluation of general nutritional conditions. A comparison has been made of the grading of nutritional status by examining physicians and the recalculated diet scores and the results are given in Table IV.

TABLE IV

Comparison of Regrading of Food Intake with Nutritional Status
(Figures given are percentages of total number of each sex)

Group	Nutritional Status	Regrading of Food Intake			
		Excellent	Good	Fair	Poor
Girls	Excellent	30.8	16.8	3.8	1.0
	Good	12.2	11.2	2.4	0.4
	Fair	9.4	8.4	2.1	0.4
	Poor	0.6	0.6	0.0	0.0
Boys	Excellent	37.3	23.1	3.5	0.8
	Good	5.4	6.5	0.4	0.0
	Fair	11.5	8.1	1.9	0.4
	Poor	0.4	0.0	0.8	0.0

Distinctions between excellent and good, whether for nutritional status or for diet score, are relatively insignificant, as compared with differences between excellent and good on the one hand and poor on the other. For practical purposes excellent and good can be considered to be one grade. On this basis 71 per cent of the girls and 72.3 per cent of the boys had excellent or good nutritional status and excellent or good food supplies; corresponding figures from the previous grading were, girls, 56.2 per cent and boys, 57.2 per cent. It cannot be said that regrading the diet score has brought about better correlation between the diet scores and nutritional status; a true correlation cannot be secured when the bulk of the subjects are in the top grades in respect to both qualifications. It can, however, be said that the regrading of the food intakes, even on a limited basis, has made the interpretation of the food consumption more consistent with the physical evaluation of nutritional status. In this group of students only 1 per cent of the girls and none of the boys were considered as having poor health; the nutritional status, as judged by physical examination, was also satisfactory for practically all of the group. The assessment of thiamin and ascorbic acid supplies, on the basis of recommended allowances, appeared quite inconsistent with physical findings. No proof is available that the standards used in the recalculation are more reliable than the recommended allowances but their use has made the two sets of data more consistent.

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Facial Paralysis in Relation to Poliomyelitis

A Study of a Family Outbreak

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THE recorded studies of epidemics of poliomyelitis reveal the occurrence of cases of the bulbar type in which the cranial nerve nuclei have been attacked by the poliomyelitis virus. According to Wickman (1) Medin was the first to mention involvement of the cranial nerves as a not infrequent complication of poliomyelitis and to associate certain isolated cranial nerve palsies with this disease. Among 65 cases, Medin noted involvement of the facial nerve (VII) in 9 cases, of the hypoglossal (XII) in 5, of the abducent(VI) in 6, of the spinal accessory (XI) in 4, of the oculomotor (III) in 3, of the trigeminal (V) in 1 and of the vagus (X) in 2. Wickman also states that in the bulbar type of paralysis the VII nerve is most frequently attacked, both branches of this nerve to the upper and lower parts of the face being implicated as a rule; that the paralysis may be partial, with complete or practically complete recovery later, but that there may be some residual paralysis. In his study of the Swedish epidemic of 1905 (2), he noted 34 patients with *combined* cranial and spinal nerve involvement and 22 patients with cranial nerve involvement *alone* in a total of 868 cases. In both classes the facial nerve had the highest incidence. A New York epidemic, reviewed by Wickman, comprised 752 cases of which 27 showed facial paralysis, 14 out of 20 specified cases occurring on the right side. This figure agrees with the usual statement that 60 per cent of Bell's palsies occur on the right side.

Escardo y Anaya (3) records his observation of 54 cases of facial paralysis during four epidemics in Uruguay in the period 1912-1922. In the 1922 epidemic the number of "facial paralysis" cases was 13, of which 9 occurred on the right side, 1 on the left side, and 3 were combined with paralysis of the extremities. He was impressed with the coincidence of facial paralysis and poliomyelitis, its unusual frequency and stubbornness to treatment. This type of case illustrates the difficulty of differentiating clinically a *nuclear* from a *peripheral* lesion of the facial curve. It may be that many cases of the former type are relegated to the peripheral or Bell's palsy type.

The occurrence of poliomyelitis following tonsillectomy deserves mention due to the high proportion of bulbar cases. Aycock and Luther (4) in their study of this feature in reported cases during 1927 and 1928 in Massachusetts and Vermont, found 16 cases in which tonsillectomy had been performed within

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a period of from 7 to 18 days prior to the attack of poliomyelitis. Nine of these cases showed bulbar involvement and 4 had concomitant facial palsy.

In the Ottawa epidemic of 1929, reported by Lomer and Shirreff (5), of 26 poliomyelitis cases recorded as "cases admitted with paralysis" there were 4 with facial palsy. Two of the facial palsies showed no other muscle group involvement and two had an associated paralysis of upper or lower extremities.

Grinker (6) states in his text-book *Neurology* (1934) that in the past few years an increasing number of bulbar cases of poliomyelitis have been seen in

TABLE I

FACIAL PARALYSIS DUE TO POLIOMYELITIS

Sex	Age	Date of onset 1937	Prodromal symptoms	Signs of onset	Concomitant signs and symptoms
F.	20	Aug. 11	Sore throat 2-3 days before onset	Complete R. facial paralysis	Right internal strabismus
F.	8	Aug. 12	Nil	Complete R. facial paralysis	Right internal strabismus
M.	4	Aug. 15	Sore throat with slight fever	Complete L. facial paralysis	Left internal strabismus
F.	4	Aug. 19	Nil	Complete L. facial paralysis	Weakness of lower limbs with diminished knee reflexes
M.	3	Aug. 22	Slight sore throat	Complete R. facial paralysis	Right internal strabismus
F.	35	Aug. 23	Nil	Complete R. facial paralysis. Partial amaurosis of R. eye	Tingling sensations in both arms and numbness of R. half of face
M.	7	Aug. 24	Mild sore throat 2-3 days before onset	Complete R. facial paralysis	Nil

young adults. This statement is confirmed by the Ontario experience as noted in the Annual Report of the Ontario Department of Health for 1930 and in the Report on Poliomyelitis in Ontario, 1937 (7). In the latter outbreak 19.8 per cent of the paralytic cases were bulbar in type but further details are not given regarding the particular nerves involved. Of 9 cases in which tonsillectomy was performed within a month of onset 6 were paralytic cases, 4 being of the bulbar type.

In the Melbourne epidemic during 1937-38 (8), there were in all 373 cases, of which 44 were diagnosed as bulbar in type; 18 of these or 41 per cent showed facial palsy. The preliminary report of poliomyelitis in Detroit in 1939 estimates that about 25 per cent of the paralytic cases were of the bulbar variety.

An outbreak of poliomyelitis in an orphan asylum in Syracuse during the early spring of 1939 is reported by Silverman (9). Six cases occurred, of which one was a female child aged 21 months, who after 11 days' residence in the orphanage was transferred to the City Hospital on account of gonococcal

vaginitis, and was there found to have a right-sided facial paralysis. A history of fever during her residence in the orphanage was not elicited but poliomyelitis virus was recovered from the faeces 5½ weeks later. The author was reminded of two previous cases of poliomyelitis which showed Bell's palsy as a sequel to the acute attack.

Not only are cases of facial palsy being recognized as the sole manifestation during epidemics of poliomyelitis but there are recent reports of small outbreaks of an epidemic nature. Two reports of French authors may be cited:

Lavergne, Abel and Kissel (10) state that a facial paralysis may be the only sign of poliomyelitic infection, that this type of monoplegia although infrequent is not exceptional, and that the paralysis remains flaccid and never results in contracture. Cases of this type may also occur in epidemic form as in the 6 cases recorded by Nobécourt and the 7 cases noted by Stern.

Kissel (11) in a communication to the Société de Neurologie de Paris on June 2, 1938, describes a small outbreak of 6 cases of acute bulbar-spinal poliomyelitis in the village of Martigny-les-Bains, near Neuchateau in the Vosges. This outbreak, in a population of 1050 persons, is of interest because one of the fatal cases had an accompanying facial paralysis and also one of the other two survivors showed a facial paralysis, clinically of the "peripheral" type. Another interesting feature is that the outbreak was preceded by a series of 7 cases of facial paralysis. They were at first regarded as facial paralysis *a frigore* i.e. Bell's palsy, but since 4 of them had concomitant involvement of the VI cranial nerve and were followed by an undoubted outbreak of poliomyelitis, it is considered highly probable that the cases of facial paralysis were of poliomyelitic nature, affecting the nuclei of the VI and VII nerves. Table I has been compiled from the clinical accounts of these cases given in Kissel's paper. (See Table I, page 72).

The onset of the paralyses occurred from August 11th to 24th and in 4 cases sore throat appeared as a prodromal symptom two to three days before the onset. Unfortunately there is no record of a follow-up investigation to determine the presence of residual paralysis.

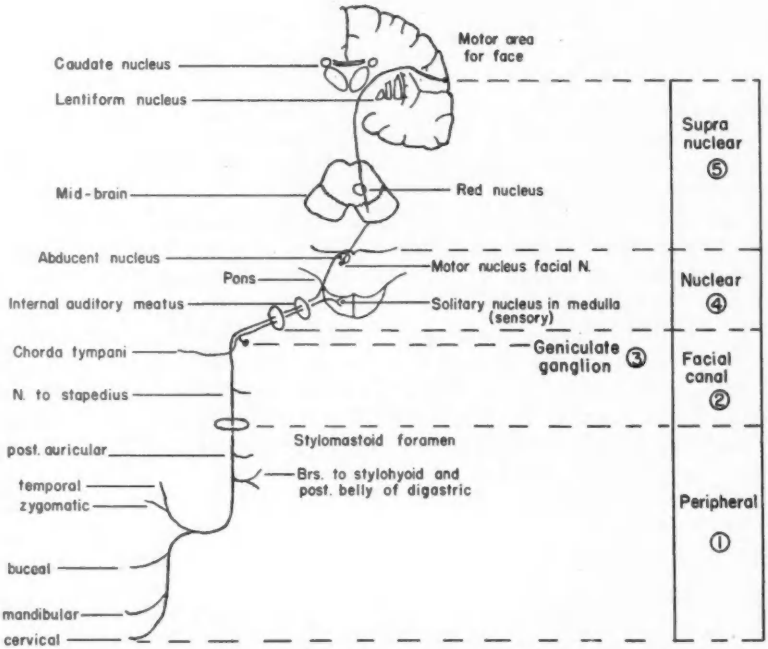
Anatomical Considerations in Relation to Bell's Palsy

It is recognized that the virus of poliomyelitis may attack the motor nuclei of the cranial nerves as well as the anterior horn cells in the spinal cord. In this connection it is worthy of note that the cranial nerve nuclei are regarded as the analogues of the anterior horn cells.

Since the facial nerve (VII) is more often involved in poliomyelitis than any other cranial nerve, a knowledge of its origin and course is necessary in order to appreciate the types of facial paralysis. Arising from its nucleus in the inferior and dorsal part of the pons, the fibres of the facial nerve follow a devious course encircling the nucleus of the abducent nerve (VI) and emerging at the lower border of the pons, near the upper end of the inferior cerebellar peduncle. The facial nerve then passes into the internal auditory meatus along with the auditory nerve (VIII). At the bottom of the meatus it

turns sharply and enters the bony facial canal which conducts it through the petrous portion of the temporal bone. The nerve emerges from the skull at the stylo-mastoid foramen, curves round the styloid process and divides in the substance of the parotid gland into the terminal branches which innervate the muscles of facial expression. The chorda tympani, supplying taste sensation to the anterior two-thirds of the tongue, joins the facial nerve in the facial canal and passes back with it as far as the geniculate ganglion, situated at the bend or genu in the nerve.

Figure 1



Schema of Facial Nerve to show five possible types of facial paralysis

The type of facial paralysis is dependent on the site of the lesion:

(*a*) A supra-nuclear lesion affecting the fibres which pass to the VII nerve nucleus produces a unilateral facial paralysis but wrinkling of the forehead is still possible because this region is controlled by fibres from both sides of the brain.

(*b*) A nuclear lesion, as may occur in poliomyelitis, results in a unilateral facial paralysis very similar to the so-called Bell's palsy. Wickman (1) states: "When such a palsy appears sporadically it is invariably considered as a peripheral paralysis. Clinically to differentiate a facial nerve palsy from a facial nuclear palsy due to Heine-Medin's disease in many cases is scarcely possible. Usually the former is more marked than the latter, but the febrile stage of the

latter is the only practical distinction." Additional evidence of nuclear involvement, however, may sometimes be afforded by a concomitant internal strabismus. Hence it seems reasonable to suspect that some cases of Bell's palsy are in reality due to a nuclear lesion of the VII nerve occurring sporadically, in which the febrile reaction is slight or overlooked.

(*c*) Between the pons and the geniculate ganglion a lesion of the facial nerve produces a flaccid unilateral paralysis of the face associated usually with deafness due to the close proximity of the auditory nerve. If, however, this nerve escapes, hyperacusis may occur from paralysis of the nerve to the stapedius.

(*d*) If the lesion occurs in the facial canal below the geniculate ganglion, a Bell's type of paralysis is apt to be produced. It appears that the true Bell's palsy is due to a lesion of the facial nerve after its exit from the stylomastoid foramen, but the term is loosely used and often no attempt is made to determine the exact site of the lesion. The explanation generally given of the etiological basis for Bell's palsy is that it is due to "refrigeration" of the facial nerve as a result of exposure to draught or cold. Actually the nerve is well protected and its course is quite short from its exit at the stylomastoid foramen to its entry within the parotid gland. Beesly and Johnston (12) suggest two other theories: toxic neuritis, and herpes of the geniculate ganglion. The latter theory receives support from Grinker, who states that geniculate neuralgia, with pain behind and within the ear, is a usual, temporary accompaniment of Bell's paralysis. A sensory disturbance such as pain or anaesthesia, often appearing early and transient, is fairly common in poliomyelitis. Further, an herpetic lesion of sensory ganglia is considered by Boyd (13) to be the sensory analogue of poliomyelitis, since the pathological lesions of the nervous system and the cerebro-spinal fluid findings in herpes zoster and in poliomyelitis are similar.

Clinical Investigation

The clinical history of an acute case of paralytic poliomyelitis admitted to the Kingston General Hospital in October 1940 revealed the fact that a member of the same family had been a patient in the hospital the previous month with Bell's palsy. It was decided to investigate the possibility of a causal connection between the two cases.

At Althorpe, 8 miles from Westport, Ont., Mr. and Mrs. T. live on a farm with their six children—Gordena, age 20, Marie, age 17, Gwen, age 15, Connell, age 9, Murray, age 7, and Gerald, age 4.

Gordena, the second daughter, went to Sudbury during the summer of 1940 to visit her married sister Vera (age 23) and returned home on August 15th with a right-sided facial paralysis, 3 days after the onset.

Gwen, the fourth daughter, complained of severe pain in the right ear on Monday, September 1st, and was treated by Dr. K. at Perth (20 miles from Westport). On the following day she began to suffer from headache which became progressively worse during the week and on September 6th she found she was unable to move the right side of her face. Dr. H. of Westport examined the patient and elicited pain at the nape of the neck on attempting to flex

the head on the chest. She was admitted to the Kingston General Hospital on September 6th with a diagnosis of meningitis.

The record of the physical examination in hospital states that the pupils are equal and react to light and accommodation, but there is inability to close the right eyelid, associated with paralysis of the right side of the face. The temperature on admission was 99.6°F. but returned to normal limits on September 7th. The Wassermann test on the blood-serum was negative. The cerebrospinal fluid was clear and colourless: Pandy's test for increased globulin was negative.

The aural surgeon's report dated September 8th states: "Right membrana tympani reddened but not bulging. Tenderness on pressure in right glenoid fossa. It is possible that the facial nerve has suffered from extension of the inflammation or exudation involved in the inflamed ear. Surgical intervention does not appear to be indicated at present." The patient was discharged on September 12th, the parents being informed that the facial palsy would take some time to clear up, probably a month.

On Monday, October 7th, Murray, the second son, was sent home from school with severe abdominal pain and vomiting. Next day the boy seemed better and was playing outside but on Wednesday, October 9th, he complained of severe pains throughout the body, chiefly in the legs, and especially in the right leg. The patient was examined by Dr. H., Westport, on October 10th and a diagnosis of poliomyelitis made on October 12th. After admission to the Kingston General Hospital on October 13th, the child was put on a Bradford frame and the left leg in a splint. Next day the right leg was put in a splint. On October 20th heat was applied to the right leg and massage prescribed night and morning. The boy was discharged on November 3rd with instructions that his parents keep him on the Bradford frame for three months and retain the splint on the left leg with daily removal, massage and reapplication of the splint. A re-examination at the hospital was recommended after six weeks.

Present Condition: Visits to the farm were made on August 26 and November 22, 1941, and the present condition of the girls, Gordena and Gwen, and their brother Murray noted. A year after the attack, Murray has a flaccid paralysis of his left leg with wasting of the thigh and calf muscles, drop foot and absent deep tendon reflexes. He walks with a typical poliomyelitis gait. To a casual observer the faces of Gordena and Gwen appear normal but close inspection reveals the following features: (1) the right palpebral fissure is narrower than the left, (2) tight closure of the eyelids reveals partial obliteration of the wrinkles on the right eyelid, (3) partial obliteration of the normal furrows over the root of the nose on the right side when frowning, and (4) partial obliteration of the right naso-labial groove and lack of contour of the cheek muscles when smiling.

Discussion

In most of the family outbreaks of poliomyelitis which have been reported, the short interval (5 or 6 days) elapsing between the primary and secondary cases

suggests simultaneous or nearly simultaneous infection. Multiple cases in families are more frequent than was formerly believed if the non-paralytic, the transitory paretic and the abortive types of the disease are recognized. The *explosive* character of a family outbreak is emphasized if multiple types of the disease are noted, and this indicates a common source of infection.

The present family outbreak suggests an unusual course, a primary case followed by a secondary case and in turn by a tertiary case or cases.

There appear to be two possibilities in regard to the transmission of infection in this family:

A. If we consider the frank cases of paralytic poliomyelitis, the interval between the dates of onset of Gordena's and Gwen's illness (facial paralysis) is 16 days and that between Gwen's and Murray's illness is 36 days.

B. The other possibility supposes the existence of an abortive case or cases. On this view, Mrs. T. and her son Connell were probably infected from Gwen, the interval between dates of onset being 30 and 32 days; while Murray (paralytic case) and Marie (abortive case) may have derived their infection from their mother, the interval between dates of onset being 6 days.

TABLE II

DATES OF ONSET WITH INTERVENING PERIODS OF FRANK AND (?) ABORTIVE CASES OF POLIOMYELITIS IN MEMBERS OF THE SAME FAMILY

Name	Age	Date of onset	Nature of illness	Interval in days between dates of onset
Gordena	20	Aug. 15*	R. facial palsy	
Gwen	15	Sept. 1	R. facial palsy	16
Mrs. T.	48	Oct. 1	Influenzal symptoms: 2-3 days in bed	30
Connell	10	Oct. 3	Influenzal symptoms for a day	32
Murray	7	Oct. 7	Polio.—Left leg paralyzed	6 or 36(**)
Marie	17	Oct. 7	Sore throat one week	6

*Date of return from Sudbury to her home at Althorpe.
(**) 6 days if patient's mother is considered to be the source of infection; 36 days if patient's sister (Gwen) is considered to be the source of infection.

The probable connection between these cases is discussed under the following headings:

Incubation Period

The limits of the incubation period of poliomyelitis are difficult to determine precisely because the source of infection is not often demonstrable. The average incubation period usually given in text-books is 7 to 10 days, but Aycock and Luther (14) as a result of the investigation of 38 cases concluded that the

apparent incubation falls within a period of from 6 to 20 days. They found evidence that the infectious period of the disease may extend from the 14th day preceding the onset of symptoms to at least the 5th day of the disease. Flexner and Lewis (15) from the experimental inoculation of monkeys found the minimum incubation period to be 4 days and the maximum 33 days. Thus if we use 33 days as the maximum incubation period, we may add 5 days and consider 38 days as the maximum interval between onsets of the disease. Aycock and Eaton (16) maintain that it is reasonable to assume that the incubation period in the human disease is probably longer than in the experimental disease, on account of the difference between the entrance of the virus by natural channels and its direct introduction into the nervous system by artificial means. Thus the maximum figure of 33 days for monkeys may even be a little less than the maximum for human cases. If we use 38 days as the maximum period of time between onsets of the illness in several members of a family, it is evident that in both the possibilities of transmission of infection, already outlined, the intervals lie within this figure.

That the interval between dates of onset may be prolonged is shown by the infectivity of faeces from human cases. Trask, Vignec and Paul (17) reported the isolation of poliomyelitis virus from the stools of a child 18 months old and a contact with an older brother aged 6 years, who had contracted severe, paralytic poliomyelitis 8 days previously. The virus was isolated on the 2nd, 14th and 25th days after the onset of a mild febrile illness (abortive poliomyelitis) but not on the 43rd or 64th days.

Character of Onset

The onset of Gwen's illness is suggestive of an infection and was associated with headache and rigidity of the neck. The course of Gordena's illness was apparently afebrile, but, at the time of onset, she was away from home and may have had slight feverish symptoms. In Murray's case the onset was sudden and acute, and typical of an attack of acute anterior poliomyelitis. Mrs. T. and her son Connell suffered sharp attacks of "influenza" as they regarded it but their symptoms are also suggestive of abortive poliomyelitis, and this may have been the source of Murray's infection.

Residual Effects

The course of a "peripheral" affection of the facial nerve is in general quite short and the paralysis transient. In the two cases of facial paralysis cited in this paper, examination revealed a residual facial paralysis, slight but persisting two years* after the attack on the right side of the face.

Seasonal Incidence

The cases occurred in the late summer at a time when "refrigeration" of the "superficial part" of the facial nerve is very unlikely. Chills are very doubtful causes of facial paralysis.

**The three patients, Gordena, Gwen and Murray, were examined in August 1941 and again in August 1942.*

Unlikelihood of Coincidence

A coincidental occurrence of two cases of Bell's palsy followed by a case of paralytic poliomyelitis in the same family is highly improbable.

Summary

This study is concerned with a family outbreak of poliomyelitis which began by the introduction of a single case of facial palsy into a rural family, previously uninfected, and resulted in paralytic and abortive types of the disease in the other members. The dates of onset, types of illness and intervals between dates of onset among the members of the family have been considered and show two possible modes of transmission of the infection. It must be borne in mind, however, that where contact occurs in multiple cases in a family, the exposure between the individuals is generally continuous and therefore it is impossible to determine the exact time of occurrence of the infection.

Two years after the outbreak, examination showed that the two girls, Gordena and Gwen, still exhibit a slight residual paralysis of the face and that their brother Murray has a persisting flaccid paralysis of the leg. It is suggested that the virus of poliomyelitis may have involved the nucleus of the VII nerve, just as it is known to attack the anterior horn cells of the spinal cord.

Acknowledgments

I am indebted to Dr. W. T. Connell for access to the hospital records and to Dr. M. W. M. Sloane for a drawing showing the course and relations of the facial nerve.

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Production of Citrinin by Aspergillus Sp. of the Candidus Group[1]

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IN view of the marked interest in antibacterial substances of microbial origin and because of the wide field of their practical application, especially during the war, this laboratory is carrying on a series of investigations on the production of antibiotic substances of *Fungi imperfecti*.

It has been reported (9) from this laboratory that *Aspergillus sp.* of the *Candidus* group was able to produce a bacteriostatic substance similar to citrinin. Citrinin as described by Hetherington and Raistrick (2) is a yellow, crystalline substance which melts with decomposition at 166-170°C. Raistrick and Smith (7) and Oxford (6) reported that citrinin possesses bacteriostatic properties and is able to inhibit growth of *Staphylococcus aureus* in dilution of 1:50,000. Citrinin, therefore, is not as powerful a bacteriostatic agent as penicillin. Nevertheless, taking into consideration its stability in air and heat, ease of isolation and purification, and yield per litre of nutrient solution, citrinin can be considered as a promising antibiotic agent.

Description of Organism

Colonies on Czapek-Dox solution agar are at first white, floccose, spreading; later citron yellow mycelium develops at centre of colony (Ridgway Plate 16, 23′ yellow), reverse pale orange to dark brown, medium citron-yellow. Conidiophores 5-7μ thick and 150-500μ long, unseptate, with smooth colourless walls arise from submerged hyphae or as branches of aerial mycelium. Heads are white to creamy yellow, radiate and elongated, the vesicle gradually enlarged upwards 12-15μ in diameter, fertile mostly on the upper half. Sterigmata are in two series, primary 4-8μ by 3-4μ, secondary 5-8μ by 3-4μ. Many mono- or diverticilate penicilloid heads having short or long conidiophores with ordinary or vesicle-like end were also observed. Conidia smooth thin-walled, colourless, round, 3-3½μ in diameter. Grows at 45°C., liquefies gelatin, coagulates and digests milk. Sclerotia-like bodies develop when copper, lactose or mannitol is added to the medium, the reverse of the colony in this case being as a rule dark-green. It was isolated from feeds and from soil.

Material and Methods

The liquid medium used was of the following composition: $NaNO_3$, 3.00 gm.; KH_2PO_4, 1.00 gm.; KCl, 0.50 gm.; $MgSO_4 7H_2O$, 0.50 gm.; $FeSO_4 7H_2O$,

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0.005 gm.; $ZnSO_4H_2O$, 0.005 gm.; glucose, 40 gm.; distilled water, 1000 ml. Volume of medium used varied according to the size of the flask. Thus 500-ml. flasks contained not more than 200 ml. and 1-litre flasks not more than 500 ml. The medium was autoclaved for 15 minutes at 15 lb. pressure, the pH after sterilizing varying between 3.9-4.2.

The inoculum was prepared by adding sterile tap water to the sporulating 10-to-15-day-old cultures, emulsifying the contents of the tube by means of a sterile glass rod and pouring the contents into 500-ml. Erlenmeyer flasks. Equal volumes of the inoculum were then pipetted into each flask. The flasks were incubated at 26°C. or as otherwise stated, for different periods of time as required.

During the first 2 to 3 days of incubation a thin white mat usually developed on the surface of the medium and under the mat the medium began to show light orange colour. On the 5th to 7th day the mycelial mat was completely developed. It was, as a rule, finely wrinkled and abundantly dotted with golden, orange or cherry-red droplets, at which time the pH of the metabolism solution was usually 7.0. Further incubation did not change greatly the picture of the mycelial mat. However, the metabolism solution attained a darker colour and the pH reached 8-8.5.

Harvesting of the metabolism solution was accomplished by filtering off the mycelium, first through dry cheese-cloth of known weight, then through filter paper. By acidifying the clear metabolism solution with 20 per cent HCl to pH 2.0-2.5, crude citrinin immediately precipitated in a yellow flocculent mass. The acidified solutions were kept overnight in the refrigerator (4°C.) and next morning the precipitates were filtered off on filter paper of known weight, washed with cold water, dried at 105°C. overnight and weighed. Usually Whatman No. 40 filter paper retains most of the citrinin. Analyses of the metabolism solutions for reducing sugars were made according to Bertrand's volumetric method.

The differences in mycelial growth, production of citrinin and consumption of sugar can better be illustrated if the utilized energy is expressed per unit of mycelium synthesized or citrinin produced. In the first case the ratio is called "economic coefficient" and the latter "manufacturing coefficient". Finally to obtain information on the ability of organisms to produce antibiotic substance per gram of mycelium the term "production coefficient" is suggested.

Yield of Citrinin as Influenced by Nutrition

In general it is accepted that the source of energy in nutrition of micro-organisms is a factor which influences their metabolic processes and in the majority of cases regulates the chemical nature and the proportion in the complex of the by-products of these processes. Glucose seems to be the sugar which is used in the majority of cases for the production of antibiotic substances. In this case detailed study was made of the effect of various sugars, alcohol and starch on the growth of *Aspergillus sp.* and production of citrinin. The basal medium used was the same as described above with the exception of the source of carbon. The weight of sugar was equal to 40 gm. per litre in

all cases except honey. With honey, moisture content was taken into consideration and 51 grams per litre of medium were used.

It was found that the fungus grew well on reducing as well as on non-reducing sugars, on mannitol and on starch. However, it was capable of producing citrinin only on glucose, levulose, sucrose, maltose and honey. The best yield was obtained on honey medium. (Table I.)

TABLE I

EFFECT OF DIFFERENT SOURCES OF CARBON ON GROWTH OF FUNGUS AND PRODUCTION OF CITRININ
(20 days' incubation)*

Source of carbon	Yield grams per 200 ml.		Average yield of citrinin per litre of media**
	1st sample	2nd sample	
Glucose	0.381	0.493	2.185
Levulose	0.556	0.599	2.890
Sucrose	0.439	0.703	2.755
Maltose	0.321	0.461	1.955
Lactose	0	0.036	0.090
Honey	0.792	0.911	4.255
Mannitol	0	0	0
Starch	0	0	0

*Temperature of incubation in all tables is 26°C. unless otherwise stated.
**The yield of citrinin in all tables refers to yield of crude citrinin.

When a good mycelial mat was developed on one sugar, the metabolism solution harvested and the mat reflooded with medium containing a different sugar, the production of citrinin was usually lower than when it was reflooded with the original solution. The results of this experiment are summarized in Table II.

TABLE II

EFFECT OF REFLOODING OF MYCELIAL MATS WITH DIFFERENT MEDIA ON YIELD OF CITRININ
(Yield of citrinin in grams per one litre, 20 days' incubation)

Mats developed on	Mats reflooded with		
	Glucose	Sucrose	Honey
Glucose	2.562	2.240	2.130
Sucrose	3.342	3.790	3.537
Honey	2.193	2.904	3.190

To investigate the influence of concentration of glucose on the growth of fungus and production of citrinin, media containing from 4 to 22 per cent glucose were prepared. The results of this experiment are summarized in Table III which indicates that the fungus can tolerate 22 per cent concentration and still produce 2 gm. of citrinin per litre of medium. The best yield obtained was with an 8 per cent concentration.

In order to throw some light on the influence of source of nitrogen on growth

TABLE III

EFFECT OF CONCENTRATION OF GLUCOSE ON GROWTH OF FUNGUS AND YIELD OF CITRININ
(200 ml. incubated for 20 days at 28°C.)

Glucose %	Weight of mycelium (grams)	Weight of citrinin (grams)	Average yield of citrinin per litre (grams)
4	1.95	0.579	2.895
6	2.90	0.768	3.840
8	3.82	0.772	3.860
10	4.50	0.651	3.255
12	4.42	0.592	2.960
14	4.46	0.513	2.565
16	4.56	0.452	2.260
18	4.06	0.368	1.840
20	4.01	0.365	1.825
22	3.63	0.418	2.090

of mycelium and production of citrinin, the fungus was grown on media containing combinations of organic and inorganic sources of nitrogen as well as each ingredient separately. The amount of nitrogen added per litre of medium in all cases was equal to the weight of nitrogen in three grams of $NaNO_3$. The cultures were incubated for 12 days at 28°C. and results obtained are summarized in Table IV. Data presented indicate that metabolic processes of the organism were greatly influenced by the source of nitrogen. Thus cultures containing NH_4NO_3 with original hydrogen ion concentration pH of 3.9-4.0 after 12 days' incubation increased the concentration to pH 1.6, whereas cultures containing asparagin lowered it to pH 7.2. The highest yield of citrinin was produced by $NaNO_3$ and the lowest by NH_4NO_3.

TABLE IV

EFFECT OF DIFFERENT SOURCES OF NITROGEN ON GROWTH OF MYCELIUM AND YIELD OF CITRININ
(Incubated 12 days at 28°C.)

Media	pH	Yield grams per 500 ml.		Average yield of citrinin per litre
		Weight of mycelium	Weight of citrinin	
(Basal)	6.7	3.05	0.402	0.804
(Basal) + Asparagin	7.2	2.20	0.302	0.604
(Basal − N) + Asparagin	7.0	2.60	0.377	0.754
(Basal) + Peptone	5.8	1.80	0.198	0.396
(Basal − N) + Peptone	4.2	2.10	0.053	0.106
(Basal − N) + NH_4NO_3	1.6	2.15	0.037	0.074

Investigations carried on by various workers during the last two decades indicate that heavy metals in the majority of cases are indispensable in normal nutrition of micro-organisms. The object of this experiment, however, was not a detailed study with recrystallized salts but simply to show the influence of heavy metals under manufacturing conditions on production of citrinin.

The weight of metal used singly or in combination was equal to the weight of iron in 0.01 gm. of $FeSO_4$.

Data summarized in Table V indicate that the physiological processes of the organism were influenced differently by different metals or different combinations of metals. Thus the following order of metals was established: (1) influence of metals on hydrogen ion concentration of the metabolism solution after 20 days of incubation, starting with the highest concentration: Zn > Fe > Mn > Cu and combination of metals Fe + Mn > Fe + Cu > Fe + Zn, (2) influence on production of mycelium per litre of medium: Fe > Cu > Mn > Zn and combinations of metals: Fe + Zn > Fe + Mn > Fe + Cu, (3) influence upon production of crude citrinin per litre of medium: Fe > Mn > Cu > Zn and combination of metals: Fe + Zn > Fe + Cu > Fe + Mn. It is of interest to note that Zn alone produced the most acid metabolism solution, the lowest yield of citrinin and the lowest weight of mycelium per litre of solution, whereas in combination with Fe it gave the best results so far obtained.

TABLE V

EFFECT OF HEAVY METALS ON GROWTH OF FUNGUS AND YIELD OF CITRININ
(Incubated for 20 days)

Media	pH	Weight grams per 500 ml. medium			Economic coeff.	Manufact. coeff.	Production coeff.
		Weight of mycelium	Weight of citrinin	Sugar consumed			
Basal + Fe.....	7.0	3.65	1.009	15.92	0.229	6.33	2.77
Basal + Zn.....	5.10	2.30	0.175	14.70	0.160	1.19	0.74
Basal + Cu.....	7.50	2.55	0.514	13.21	0.193	3.90	2.01
Basal + Mn.....	7.10	2.35	0.744	11.90	0.197	6.25	3.12
Basal + Fe + Zn..	7.30	4.14	1.553	19.73	0.210	7.87	3.75
Basal + Fe + Cu..	6.70	2.90	0.983	13.21	0.219	7.44	3.39
Basal + Fe + Mn.	6.70	2.93	0.680	11.57	0.253	5.87	2.32

$$\text{Economic Coefficient} = \frac{\text{Weight of mycelium}}{\text{Weight of sugar consumed}}$$

$$\text{Manufacturing Coefficient} = \frac{\text{Weight of citrinin produced}}{\text{Weight of sugar consumed}} \times 100$$

$$\text{Production Coefficient} = \frac{\text{Weight of citrinin produced}}{\text{Weight of mycelium}} \times 10$$

Influence of Temperature and Time of Incubation on Production of Citrinin

The influence of temperature on production of citrinin by *Penicillium citrinum* Thom has been investigated by Hetherington and Raistrick (2). The optimum temperature suggested was 24-26°C. Waksman and Horning (10) in a study of the distribution of antagonistic fungi in nature stated that many organisms grew well at 37°C. and even 50°C.; the optimum temperature for the production of the antibiotic substance, however, was found to be 28°C. or lower. Data summarized in Table VI illustrate the influence of temperature

and time of incubation on growth and ability to produce citrinin by our fungus. Hydrogen ion concentration did not vary much in each sample between the different temperatures of incubation, the exception being found in the fourth sample of cultures incubated at 40°C. which reached pH 8.15. During the investigation it was noticed that if the hydrogen ion concentration rapidly diminished in the first 3 to 4 days' incubation, and on 5 to 6 days reached an alkaline side with pH over 8, such cultures usually did not contain any citrinin.

The data summarized under the heading of "economic coefficient" indicate that most efficient utilization of energy for cell synthesis takes place in younger cultures which gradually decrease with age. More rapid decrease is noted in cultures incubated at 40°C., whereas only gradual decrease occurred at 30°C. "Manufacturing coefficient" on the other hand indicates a gradual increase in production of citrinin in cultures incubated at 40°C. and 37°C. for 21 days; on the 28th day they showed a small decrease, whereas in cultures incubated at 30°C. they did not reach maximum production after 28 days' incubation. It is also evident that the organism is capable of producing in a shorter time more citrinin per 100 grams of sugar at 40°C. than at 37 or 30°C.

The ability of organisms to produce citrinin at different temperatures of incubation is illustrated in Table VI under the heading of "production coefficient". From the data presented it is evident that the organism when incubated for 21 days at 40°C. produced twice as much citrinin per 10 gm. of mycelium than when incubated at 30°C. for the same length of time.

TABLE VI

INFLUENCE OF TEMPERATURE AND LENGTH OF INCUBATION ON GROWTH OF FUNGUS AND YIELD OF CITRININ

Temperature °C.	pH	Weight grams per 500 ml. medium			Economic coeff.	Manufacturing coeff.	Production coeff.
		Weight of mycelium	Weight of citrinin	Sugar consumed			
		First sampling (7 days' incubation)					
30	6.95	1.43	0	5.30	0.29	0	0
37	7.00	2.05	trace	6.67	0.30	0	0
40	7.05	2.46	0.129	7.97	0.31	1.62	0.53
		Second sampling (14 days' incubation)					
30	7.20	3.16	0.240	11.20	0.28	2.14	0.76
37	7.20	2.98	0.363	11.50	0.26	3.15	1.22
40	7.20	4.26	0.552	17.60	0.24	3.14	1.30
		Third sampling (21 days' incubation)					
30	7.65	4.68	0.602	17.51	0.27	3.44	1.28
37	7.60	4.21	0.793	18.85	0.22	4.21	1.88
40	7.80	3.46	0.875	19.89	0.17	4.40	2.53
		Fourth sampling (28 days' incubation)					
30	7.50	4.60	0.829	18.67	0.25	4.44	1.80
37	7.40	3.80	0.714	19.02	0.20	3.75	1.85
40	8.15	3.12	0.763	19.89	0.16	3.84	2.45

See footnotes for Table V.

It is of interest to note that in the case of the 40°C. lot the maximum growth

of mycelium was reached on the 14th day of incubation, whereas maximum production of citrinin was obtained only after 21 days' incubation. During these last 6 days of incubation only 2.29 gm. of sugar was consumed and increase in weight of citrinin produced amounted to 323 mg. During the same period of incubation weight of mycelium decreased from 4.25 gm. to 3.46 gm., a decrease of 860 mg. From the data obtained it may be suggested that at least a partial formation of citrinin may be attributed to autolysis of mycelium.

Table VII indicates that the highest yield of citrinin was obtained after 28 days' incubation when glucose and honey were used as sources of energy. In the case of cane sugar the maximum yield was not reached after 32 days' incubation.

TABLE VII

EFFECT OF SUGARS AND LENGTH OF INCUBATION ON YIELD OF CITRININ

Days incubation	Weight grams per litre of medium		
	Glucose	Cane sugar	Honey
8	0.687	0.300	0.870
14	1.967	2.207	2.313
20	2.539	3.065	3.735
24	3.900	3.631	3.985
28	4.189	3.805	4.250
32	3.912	3.815	4.025

Strain Specificity of Aspergillus sp.

The specificity of the strains of *P. notatum* in production of antibacterial substances both quantitatively and qualitatively has been reported by many investigators (1, 4, 5, 11). This same phenomenon was observed with our fungus. Twelve strains selected to illustrate this case, as shown in Table VIII, vary considerably in their yielding capacities. However, the differences appeared to be quantitative rather than qualitative in nature. It is of interest to note that strains isolated from soil had, as a rule, a lower yielding capacity,

TABLE VIII

PRODUCTION OF CITRININ BY DIFFERENT STRAINS OF *Aspergillus sp.*
20 days' incubation at 28°C.

Strain	Grams per 200 ml. medium		Average weight per litre
	1st sample	2nd sample	
T-1-1	0.542	0.470	2.530
T-1-2	0	0	0
T-1-3	0.630	0.632	3.155
T-1-4	0.270	0.346	1.540
T-1-5	0.569	0.566	2.840
T-1-6	0.473	0.444	2.295
T-1-7	0.028	0.077	0.265
T-1-8	0.308	0.319	1.570
T-1-9	0.671	0.669	3.350
T-1-10	0.627	0.650	3.190
T-1-11	0.606	0.539	2.865
T-1-12	0.638	0.651	3.225

whereas strains isolated from feeds or chicken mashes had high yielding capacities.

Low-yielding strains in the majority of cases produce a thick mycelial mat with dark brown, almost black, reverse and the metabolism solution after 5-7 days' incubation showing a pH of 8 or even higher.

Purification of Citrinin

Using Hetherington and Raistrick's (2) "hot alcohol" method for purification of crude citrinin, it was found that crude citrinin contains from 1 to 2 per cent alcohol insoluble matter. The total recovery of crystalline matter amounted to 40-50 per cent of the original weight of crude citrinin. The melting point of the crystals of this preparation was 170-171°C. with decomposition.

The remains of the matter, which did not crystallize from alcohol when concentrated under reduced or normal pressure, contained some tar-like substance and some resembling decomposed citrinin. When water was poured into this concentrate, a flaky orange precipitate appeared immediately. The melting point of this orange powder was around 180°C. without definite melting point.

It is possible to increase the yield of pure citrinin by modification of the Hetherington and Raistrick method as follows. After removal of the alcohol insoluble matter, distilled water 3-4 times its volume was added to the filtrate. Citrinin crystallized into long microscopic needles or serrate plates. The crystals filtered and dried at 100°C. were golden yellow or golden buff in colour. Recovery of crystalline citrinin by this method amounted to 60-70 per cent of the original weight. The melting point of this preparation was 168-170°C.

Tauber *et al.* (8) recently suggested the use of dioxane for the purification of crude citrinin. Using Tauber's method, it is possible to obtain 70-80 per cent of the crude citrinin as pure crystalline matter. Crystals of this preparation were smaller than those obtained from alcohol and were of citron yellow colour with melting point 170°C. with decomposition.

Comparing the citrinin melting points that have already appeared in the literature with melting points of our own preparations, it is evident (Table IX) that citrinin obtained from *Aspergillus* metabolism solutions does not differ in melting points from citrinin obtained from *P. citrinum*. Furthermore, all our

TABLE IX

MELTING POINT OF CITRININ OF DIFFERENT PREPARATIONS

Method of Preparation	Authors	Melting Point °C.
Hot alcohol	Hetherington and Raistrick	166-170
" "	Hirschy and Ruoff	170-171
" "	Timonin and Rouatt	170-171
Dioxane	Tauber *et al.*	163-166
"	Timonin and Rouatt	170
Alcohol	Timonin and Rouatt	168-170
Unpurified	Timonin and Rouatt	165-168

preparations except the orange powder (residue of crystallization) gave positive reactions to Tauber's citrinin colour test (8) as well as $FeCl_3$ test. The chromatogram on MgO prepared with citrinin received from Dr. H. Raistrick did not differ from the picture of our own citrinin of dioxane preparation. Alcohol preparations, however, contain some impurities which can be removed by recrystallizing it from dioxane. According to Dr. R. H. F. Manske, citrinin of our preparation did not differ in chemical composition from that received from Dr. H. Raistrick.

The above findings indicate that crystalline matter obtained from metabolism solution of *Aspergillus sp.* is the same as that obtained from *P. citrinum* Thom metabolism solution and described by Hetherington and Raistrick.

Summary

A fungus isolated from cattle feed and identified as *Aspergillus sp.* of the *Candidus* group proved capable of producing citrinin when grown on synthetic media with glucose as source of energy. It was found that the fungus can produce good growth on glucose, levulose, sucrose, maltose, lactose, honey, cane sugar, mannitol and starch. Citrinin, however, can only be produced on glucose, levulose, sucrose, maltose, honey and cane sugar. It was also found that the source of nitrogen greatly influenced the metabolic processes of the organism, the best yield being obtained with $NaNO_3$. Iron in combination with zinc proved to be the best source of heavy metals. Times of incubation for maximum production of citrinin were found to be different for different temperatures. Thus at 40° and 37°C. maximum yield was obtained after 21 days whereas at 30° or 26°C. 28 days or more were necessary.

Isolates from different sources proved to be morphologically identical but showed great variation in citrinin-producing ability. Furthermore, even the strain with high yielding ability when grown for inoculum on different media varied considerably in production of citrinin.

Purified citrinin did not differ in chemical composition from that obtained from *P. citrinum*.

Acknowledgments

The authors are indebted to Dr. H. Raistrick for kindly furnishing a sample of citrinin and to Dr. R. H. F. Manske for chemical analysis of citrinin. They wish also to thank Dr. A. G. Lochhead for his sustained interest in the problem.

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ORAL VACCINES FOR COLDS

THE increasing sale of vaccines administered by mouth in the form of capsules or pills for the alleged prevention of colds is apt to lead physicians to believe that the administration of such preparations rests on sound scientific data. This is not the case. Furthermore, there is no known method for the prevention of common colds. Undoubtedly the common cold is of virus origin. As the virus or viruses have not been identified, it is futile to believe that it is possible to prevent common colds by a vaccine composed of bacteria commonly found in the upper respiratory tract. "Shotgun" mixtures including influenza A virus are being marketed and the public is spending money for which little or no value is obtained. Too often, physicians are impressed by very limited observations on small groups of "vaccinated" individuals. Even large-scale experiments reported by industrial physicians relating to the favourable experience of one season are often followed by negative results in a succeeding season. Controlled observations made by scientific workers on adequate numbers of individuals have demonstrated clearly that so-called "oral vaccination" is without value in the prevention of colds.

In a recent issue, the Journal of the American Medical Association[1] spoke strongly of this situation:

"Recent communications to the offices of the American Medical Association indicate that the prescription and sale of cold vaccines is again taking place on a large scale. This, in the face of the recognized lack of scientific evidence for the value of these preparations, is indication of irresponsibility on the part of some manufacturers of pharmaceuticals. The scientific evidence against the value of oral cold vaccines is overwhelming; consequently individual physicians and firms who deal in pharmaceuticals and who lend themselves to wholesale uncontrolled distribution of such preparations are perpetrating an unwarranted assault on the public pocketbook."

[1] J.A.M.A., 1944, *124*: 236.

Laboratory Supplement

ABSTRACTS OF PAPERS GIVEN AT THE CHRISTMAS MEETING OF THE LABORATORY SECTION, HELD IN TORONTO ON DECEMBER 15 AND 16, 1943

Two Cases of Ghon Lesion, with discussion of the Recognition of Primary Pulmonary Tuberculosis by X-ray

THE Ghon lesion is described, also its sequelae and complications. A case is given in which the lesion was invisible by X-ray examination but blood invasion took place, with a terminal meningitis. The authors suggest that after infection occurs there is a latent period in which the only demonstrable change may be the allergic response to tuberculin.

James Miller and Wm. D. Hay, Richardson Pathological Laboratory, Queen's University, Kingston, Ontario.

The Adaptation of M. paratuberculosis to Artificial Culture Media Prepared without the Addition of the "Essential Growth Factor"

THE acid-fast micro-organism *M. paratuberculosis* (Johne's bacillus) is characterized by the fact that it may be isolated from the natural host only when a special growth factor has been added to the medium. This so-called "essential substance" may be supplied by the heat-killed cells of certain other acid-fast bacilli or their metabolites.

After the micro-organism has been carried for various periods of time on artificial media, it apparently regains the ability to elaborate the growth factor from suitable media.

In the paper the adaptation of five old laboratory strains and seven freshly isolated strains of *M. paratuberculosis* to ordinary Long's synthetic and potato-Long's synthetic medium are described. From the comparison of the time periods required to accomplish this, the conclusion is drawn that *M. paratuberculosis* may be educated to grow on artificial media without the addition of the specific growth factor in a comparatively short time after its isolation.

It was attempted, without success, to increase the luxuriance of six adapted strains by cultivation on Dorset's synthetic medium at various pH levels.

Some changes in gross cultural appearance and biological properties observed in one strain after prolonged cultivation on plain Long's synthetic medium are mentioned.

H. Konst, Division of Animal Pathology, Science Service, Dominion Department of Agriculture, Animal Diseases Research Institute, Hull, Quebec.

Resistance to Ascaris lumbricoides L. Infection as Demonstrated Experimentally in Guinea Pigs

IT has been shown quantitatively, by counting the number of larvae reaching the lungs, that guinea pigs infected with the larval stages of *Ascaris lumbricoides* are resistant, to a degree, to subsequent infection with this parasite for at least 3 months after the initial infection. The resistance was more complete 1-3 weeks after the infection than after 3 months. Complete immunity was never demonstrated. Transfer of serum from resistant to non-resistant pigs afforded the latter slight protection. It was found, by recovering larvae from livers and lungs of resistant and non-resistant pigs on successive days following infection, that a number of larvae reached the livers but few reached the lungs of the resistant animals, whereas as many, or more larvae were recovered from the lungs of the control animals as from the livers. This suggests that the liver of a guinea pig resistant to Ascaris infection acts as a barrier to the larvae of this parasite.

A. Murray Fallis, Ontario Research Foundation, Toronto.

Shellfish Poisoning in Canada

CASES of shellfish poisoning in humans have occurred in Canada at relatively long intervals and in widely different localities on both coasts during

the past 150 years. A few deaths and several cases have been reported during the past few years. At the present time, the occurrence of poisonous mussels and clams is of some concern since these shellfish are being more widely consumed both fresh and canned.

The Fisheries Research Board and the Department of Fisheries, in co-operation with the Department of Pensions and National Health, have been keeping in close touch with the situation for the past five years. All commercial shellfish-producing areas are sampled at intervals and as soon as shellfish are found to contain more than 400 units of mussel poison per 100 grams of meat the provincial authorities are notified and the area is closed for the taking of shellfish. It has been found that, in Canada, shellfish may remain poisonous throughout the year in certain localities on both coasts. This finding is contrary to the data reported from other parts of the world.

A simplified acid aequeous method of extraction of the poison has been developed. This method is based on the extraction of 100 grams of drained shellfish meat. The extracts are assayed by intraperitoneal injection into mice and the results are expressed in terms of mouse units per 100 grams of meat. At the present time, the quarantine level adopted for use in this country has been set at 400 mouse units per 100 grams of whole shellfish meat. Comparative assays of mussel poison using Sommer's acid alcohol method and the acid aequeous method have indicated that the California quarantine level of 2 milligrams, which was based upon their epidemiological data, and the Canadian limit of 400 mouse units are of a similar order.

It has been found that for the Pacific coast butter clam the poison is not, as has been reported, concentrated in the digestive gland. As a matter of fact, considerably larger amounts of poison were found in the mantle or the foot than in the digestive gland while up to 90 per cent of the poison may be located in the siphon.

This year, for the first time, specimens of the soft shell clam, *Mya arenaria,* were found to be dangerously toxic in the Passamaquoddy Bay area on the Atlantic coast. Mya toxicities as high as 11,000 units were noted.

J. Gibbard and J. R. Naubert, Laboratory of Hygiene, Department of Pensions and National Health, Ottawa; R. E. Foerster and J. P. Tully, Fisheries Research Board, Nanaimo, B.C.

Transmission of Salmonella pullorum by Flies

In the first two experiments, the chicks died from pullorum disease after being exposed to flies that had fed on infected feed and dead chicks. The possibility of some of the chicks having eaten infected flies could not be excluded.

The next two experiments, in which later subcultures were used, did not result in any of the chicks becoming infected, although in experiment no. 3 the chicks died as the result of chilling.

A small number of chicks died in the fifth experiment as a result of feeding chick mash which had been exposed to infected flies. These flies were fed to another group of chicks, from some of which the organism was also recovered.

Subsequent failure to infect chicks by feeding and injecting relatively large amounts of bacterial suspension suggested that the small number infected in the later experiments was probably due to lowered virulence of the infective agent. The use of infected chicks rather than culture would appear to offer a greater assurance of virulence in experiments of this type.

S. pullorum was recovered from the feet and wings of flies immediately after exposure to bait and six hours later. It was recovered from the intestinal tract up to five days after exposure. Cultures were not made after the times indicated in either case.

Ronald Gwatkin and Chas. A. Mitchell, Division of Animal Pathology, Science Service, Dominion Department of Agriculture, Animal Diseases Research Institute, Hull, Quebec.

A Mouse Protection Test for Cholera Vaccine

THE protective efficacy of cholera vaccine can be readily demonstrated in unselected white mice. In testing a vaccine, two groups of 15-20 mice are given intraperitoneally two doses of vaccine, one week apart. A fortnight after the second immunizing dose they are challenged with 5 and 10 m.l.d.'s respectively of a single strain of *V. cholerae* suspended in 5 per cent mucin. Since cross-protection between Ogawa and Inaba-type strains appears complete in mice so treated, the challenging strain can be of either type. It is recommended that vaccine acceptable for human use should protect 100 per cent of vaccinated mice against 5 m.l.d.'s, or 80 per cent against 10 m.l.d.'s, of *V. cholerae*. Several lots of phenol-killed, pooled cholera vaccine tested at various times up to twenty-six months after preparation showed retention of a high degree of mouse-protecting capacity for two years.

L. E. Ranta and C. E. Dolman, Connaught Laboratories (Western Division), University of Toronto.

The Survival of E. typhosa in Cheddar Cheese Manufactured from Infected Raw Milk

CHEDDAR cheese was manufactured by a commercial process. Each vat of raw milk infected with *E. typhosa* was manufactured into two 12-pound cheese. These were ripened for two weeks at 58-60° F. At that time, one cheese of each pair was continued in storage at the same temperature while the other was stored at 40-42° F.

In general, it may be stated that, under experimental conditions, most of the *E. typhosa* were dead in cheese stored at 58-60° F., after a storage period of three months, whereas similar cheese stored at 40-42° F. retained viable *E. typhosa* for at least six months and in a majority (7 out of 10) for ten or more months. The size of the inocula used to infect the raw milk did not seem to be a factor. There does not seem to be any correlation between the acidity and the viability of *E. typhosa* in the cheese. All of the cultures recovered at the conclusion of the experiment were tested for identity by serological and biochemical methods and all were found to be in the smooth Vi phase. None of the strains had reverted to the rough or W form.

A. G. Campbell and J. Gibbard, Laboratory of Hygiene, Department of Pensions and National Health, Ottawa.

Bacteriostatic Activity of Citrinin in Vitro

DURING the course of investigations on the potency of citrinin *in vitro* it was found that citrinin exerts bacteriostatic activity on Gram-positive organisms only. Assay media containing 1 per cent of glucose demonstrated higher values of potency of citrinin than plain media. Furthermore, it was demonstrated that crystalline citrinin obtained by different methods of purification differed in their bacteriostatic potencies.

Addition of fresh horse serum to the assay medium reduces the bacteriostatic potency of citrinin, whereas p-amino-benzoic acid does not interfere with it.

Two mgs. of citrinin dissolved in 0.5 ml. of solution and injected intraperitoneally proved to be lethal to 20-gm. mice. All mice survived when only 1 mg. of citrinin was injected. Therefore the minimum lethal dose lies somewhere between 1 and 2 mgs. of citrinin.

M. I. Timonin, Division of Bacteriology and Dairy Research, Science Service, Department of Agriculture, Central Experimental Farm, Ottawa.

Observations on the Antigenic Properties of Staphylococcus Enterotoxin

THE physical, chemical and antigenic properties of staphylococcus enterotoxin have been the subject of many discrepant reports. This situation may be due to the beta-toxin having been at times confused with the enterotoxin; and also to inadequate differentiation between the development of tolerance and of immunity in test animals. A group of five persons, whose respective

minimal reacting doses of enterotoxin had been established by preliminary ingestion experiments, were given a series of small subcutaneous injections of filtrate prepared from a potent food-poisoning strain. Two volunteers, who had each reacted markedly to 1.5 cc. of filtrate taken on several occasions over a period of many months, received 4 and 5 injections respectively of untreated filtrate obtained by growing the strain on a soft agar proteose-peptone medium at room temperature for 3½ days, under which circumstances no detectable alpha- or beta-toxins were formed. The injections were given over a period of 19 days, and totalled 0.2 cc. in one case, and 0.5 cc. in the other. Ten days after the final injection, they were able to take 3.0 cc. of filtrate without any reaction. About four months later, both again took 3.0 cc. with impunity. After a further series of 4 small injections, one of these subjects had no ill effect from taking 5.0 cc. of filtrate, although 1.5 cc. amounts of filtrates of similar potency had previously caused violent vomiting and diarrhoea.

Three other volunteers had their minimal reacting doses to a potent filtrate determined. They were then given 4 small subcutaneous injections of a filtrate prepared from the same enterotoxigenic strain, using a similar medium, but incubating at 37° C. for 40 hours in an atmosphere containing 30 per cent carbon dioxide, and subsequently treating with 0.5 per cent formalin until no detectable alpha-toxin remained. Each person received a total of about 0.2 cc. of this toxoid over a period of 12 days, and within a day or two thereafter began to test their degree of resistance to enterotoxin taken by mouth. One subject, who had suffered gastro-intestinal derangement with diarrhoea for 36 hours after ingestion of 0.75 cc., was able, after the toxoid injections, to take 2.0 cc. of the same filtrate without deleterious effect. Another subject, made violently sick by 0.75 cc. of filtrate before the series of injections, afterwards had no reaction to 1.5 cc., and was only slightly affected by 2.0 cc. A third subject initially had a severe reaction to 1 cc. of filtrate, but was subsequently able to take 2.5 cc. without effect, although 3 cc. still caused vomiting.

To summarize, five persons treated with a few small subcutaneous injections of filtrate containing staphylococcus enterotoxin developed resistance to at least twice the dose of enterotoxin which had formerly made them ill; while one of the group who received a small series of supplementary injections four months later, became resistant to more than three times the former minimal reacting dose of enterotoxin. In view of the fact that the minimal reacting dose of enterotoxin for an untreated person appears to remain constant within very narrow limits, results such as the foregoing are held to indicate that enterotoxic filtrates are antigenic for man, and that some measure of active immunity against the enterotoxin can be induced by a series of subcutaneous injections of suitably prepared filtrate. Attempts will be made to achieve somewhat higher degrees of immunity by injecting larger dosages over a longer period.

In the cat, whose normal susceptibility to enterotoxin is relatively low, the development of immunity is less striking; but results pointing to the same general conclusion as to the antigenicity of staphylococcus enterotoxin have been obtained in cats given numerous intravenous injections of enterotoxic filtrate.

C. E. Dolman, Connaught Laboratories (Western Division), University of Toronto, and Department of Bacteriology and Preventive Medicine, University of British Columbia.

Factors of Importance Regarding a Laboratory Examination for Rabies

APPROXIMATELY only 60 per cent of specimens sent to the laboratory for rabies examination are regarded as positive. This relatively low percentage can be attributed to the fact that rabies is not an enzootic disease in Canada. During outbreaks health officials and the general public are

prone to suspect the disease on very slight evidence. This is not the case in countries where rabies occurs more or less constantly.

The method of examination is described and important factors stressed. These include: (1) The desirability of using a stain that is little affected by the condition of the brain. (2) The necessity of being able to distinguish true and false Negri bodies. Tissue reactions that may be mistaken for Negri bodies are mentioned. (3) Because Negri bodies sometimes occur in relatively localized areas and in groups, it is necessary to examine a large number of preparations before one is able to say these are not present. (4) The importance of considering possible bacteriological contamination of the brain. In making animal inoculations representative portions of the brain should always be treated to eliminate possible contamination in order that inoculum may be prepared from these tissues if necessary.

P. J. G. Plummer, Division of Animal Pathology, Science Service, Dominion Department of Agriculture, Animal Diseases Research Institute, Hull, Quebec.

The following papers, given at the Christmas meeting but not abstracted here, will be published in full in early issues of the JOURNAL:

A Chronic Typhoid Carrier. A. R FOLEY, Epidemiologist, Ministry of Health and Social Welfare, Province of Quebec.

Chairman's Address: *The Laboratory and Social Medicine.* F. T. CADHAM, Professor of Bacteriology and Immunology, University of Manitoba, and Director of Laboratories for the Province of Manitoba.

Glanders in Man. C. D. MCGILVRAY, Principal, Ontario Veterinary College, Guelph.

REPORT OF THE COMMITTEE ON CHEMICAL WATER STANDARDS

CANADIAN INSTITUTE OF CHEMISTRY AND CANADIAN PUBLIC HEALTH ASSOCIATION

THE annual meeting of the committee was held in Toronto on April 6, 1943.

The vacancy caused by the resignation of Dr. Gauvin has been filled by the appointment of Dr. Jacques Archambault of the Division of Laboratories, Ministry of Health of the Province of Quebec, Montreal.

The office of secretary, occupied by Dr. C. A. MacConkey to the end of June, 1943, has been taken over by Mr. D. Wolochow of the National Research Council.

The membership of the committee is, therefore, as follows: Mr. H. A. Leverin (Chairman), Dr. Jacques Archambault, Mr. C. H. Bayley, Mr. A. R. Bonham, Capt. A. V. DeLaporte, Prof. O. J. Walker, and Mr. D. Wolochow (Secretary).

A modified method for phenol determination and a proposed method for the determination of small quantities of chromium in water and sewage have been drawn up and are being tested in use.

The chairman, who is also a member of the Joint Editorial Committee of the American Water Works Association and the American Public Health Association, attended a meeting of that committee in Cleveland on June 16th and 17th of this year. The work of members of this committee, like that of our own, has been much hampered by more pressing matters connected with the war, so that the completion of the work on the ninth edition of *Standard Methods of Water Analysis and Sewage*, which has been in progress during the past three years, has been much delayed, and at the time of the meeting some members had not submitted their reports on the work

assigned to them. The work of your committee, however, is completed and the report on it awaits final revision by the Joint Editorial Committee as a whole. It was agreed that all work must be completed and copies of reports thereon distributed to the committee members not later than September 15th. This, however, does not appear to have been possible as no such copies have so far been received by the chairman. It is therefore uncertain when the book will be in shape for the printer.

Dr. O. J. Walker has suggested that your committee investigate the possibility of eliminating sodium bicarbonate which is present in many well waters in the Province of Alberta. It has an adverse effect on the health of young pigs. This matter will be discussed at our next annual meeting.

D. WOLOCHOW, *Chairman.*

REPORT OF THE COMMITTEE ON BACTERIOLOGICAL METHODS OF EXAMINATION OF WATER AND SEWAGE

DURING the past two years the pressure of routine work has prevented the members of the Committee on Bacteriological Methods of Examination of Water and Sewage from undertaking any intensive study of questions relative to water examination. The committee has, however, followed closely the work of revision of the Eighth (1936) Edition of *Standard Methods of Water Analysis,* published by the American Public Health Association and the American Water Works Association, and adopted by the Canadian Public Health Association. While this revision was in progress, a comparative study of a new medium for detection of coliform organisms, lauryl sulphate tryptose broth, was made by a number of collaborating laboratories in the United States and Canada, and the results were so satisfactory that this medium has been included in the proposed revision of *Standard Methods* as an alternative to lactose broth as a primary and secondary medium for the examination of all waters except filtered, treated and filtered-treated waters; and its use in the examination of this latter group of waters is permitted, provided it has been shown by actual test to yield results that are comparable with those secured through the use of lactose broth.

Other more important changes appearing in the proposed revision are the permission to employ the so-called "confirmed test" in the examination of *all* waters (it will be recalled that the present *Standard Methods* require the use of the "completed test" in the examination of certain waters); and the permission to use the medium generally employed in the examination of milk samples, tryptone glucose agar (without added milk), as an alternative to nutrient agar, for securing plate counts of water samples.

Numerous minor changes in media, methods and their applications, are also included in the revision in its present state of preparation.

Each member of the committee has had the opportunity to study the proposed revision and to suggest changes or corrections. With the exception of minor corrections, the revision was accepted by all members of the committee. If, prior to publication, further additions or alterations of any importance are contemplated, the committee will be informed and consulted.

Upon completion of the revision and its publication as the Ninth Edition of *Standard Methods of Water Analysis,* the committee will propose that this Laboratory Section consider recommending adoption of the bacteriological methods thereof for use in Canadian laboratories.

NORMAN J. HOWARD, A. GRANT LOCHHEAD, and M. H. MCCRADY, *Chairman.*

Vital Statistics

SUMMARY REPORT OF THE DOMINION-PROVINCIAL CONFERENCE ON VITAL STATISTICS

THE Dominion-Provincial Conference on Vital Statistics which was held in Ottawa on October 7-9, 1943, was the first such gathering since 1918, when the plans were formulated for the setting up of the existing national system of vital statistics.

Owing to the absence from the city of the Honourable James A. MacKinnon, Minister of Trade and Commerce, the conference was officially opened by Mr. Oliver Master, Acting Deputy Minister. After welcoming the representatives of the Provincial Departments of Health and those of other Canadian government departments and national organizations interested in the improvement and utilization of vital statistics, also Dr. Halbert L. Dunn, Chief Statistician for Vital Statistics in the United States Bureau of Census, and Secretary-General of the Inter-American Statistical Institute, and Mr. W. C. Welling, Director of Vital Statistics for the State of Connecticut and President of the American Association of Registration Executives, the Minister's address stated in part:

"It is unnecessary in this gathering to emphasize the importance of our national system of vital statistics. Not only are vital records essential as an aid in preventing crime, in facilitating the transfer of property and in promoting the security and moral tone of social life in general, but statistically they lie at the very basis of sanitation and public-health policies, and afford a measure of national efficiency from a most important point of view, namely, the biological numbers, reproductive force, and vitality of the people.

"Vital statistics is a subject which, though of paramount interest from a local-provincial standpoint, requires the broadest possible treatment in order to reap the full benefits of its study. It becomes the duty, therefore, not only of the local authorities to take appropriate action, but of the Dominion as a whole to check, collate and compare results, so that not only may town be compared with town, but province with province, and Canada as a whole with other countries.

"In the twenty-five years that have elapsed since the last conference, many new problems have arisen. The present world conflict has created many urgent problems of social health and welfare, complex in character, while the scheme now being formulated for health insurance has made very comprehensive demands upon our vital statistics organization and clearly demonstrates that the time has come for the serious consideration of all matters pertaining to our vital statistics structure."

The Chairman, Mr. S. A. Cudmore, Dominion Statistician, in his opening remarks stressed the supreme importance of birth registration. He stated that in 1918 when our present system was instituted:

"Hundreds of thousands of Canadians could not supply legal proof that they had ever been born; indeed, even today many of our older people cannot from their own records establish their claims to Old Age Pensions, with the result that the Government had to impose upon the Bureau of Statistics the task of searching the records of the older census so that such persons may establish proof of age in cases where the Family Bible is not available. At the present time no fewer than fourteen clerks are constantly employed in the Bureau in trying to make up for those deficiencies of the past. Even so, many of our older people, and indeed many of our younger people, will suffer for many years to come from the lack of adequate official records of their births. I recall that even as recently as 1911 an investigation showed that some 25 per cent of the infants who had been baptized in certain Toronto parishes had never been registered as births.

"Since the inauguration of the present system of Dominion-wide vital statistics conditions have greatly improved and a recent comparison of birth registrations with the Census records of the Census of 1941 indicates that at the present time we are registering probably 97 to 98 per cent of the births. For this improvement in registration Canada is greatly indebted to the day-by-day work of the Provincial Registrars, but registration is after all only the start of the work. Vital statistics require not only complete registration but comprehensive compilation and interpretation of the records.

"Statistics, someone has said, are of use not only in recording the facts of the present, but also in determining what shall be in the future—the goal to which we shall work and the ideal at which we shall aim. New vistas of a healthier and happier Canada rise before

our eyes in connection with the present movement toward social security.

"During the last war we heard a great deal about making Canada a land fit for heroes to live in. I trust that after the present war we shall make it a land fit not only for heroes to live in but for those of us who are not heroes to live in and to live longer in, with better health and increased efficiency and well-being."

Dr. Dunn, of the United States Census Bureau at Washington, stressed the need of cohesion and the integration of vital statistics with other statistics. He paid tribute to Canadians and their statistical achievements and mentioned freely certain respects in which it was evident the Dominion had forged ahead of the United States.

The importance of registration of Indians and the adoption of standard forms for their registration throughout Canada was brought to the attention of the delegates by Dr. P. E. Moore, of the Indian Affairs Branch, Medical Services, and Dr. G. J. Wherrett, Secretary of the Canadian Tuberculosis Association. As a result of the deliberations it was resolved that standard national forms should be prepared by the Dominion Bureau of Statistics for the separate collection and compilation of vital statistics respecting the Indians of Canada who are wards of the Dominion Government; and that the system, which has been in operation in British Columbia since 1916, be given one year's trial in all provinces.

The important problem of registration and classification of stillbirths and foetal deaths was ably discussed by Dr. Ernest Couture, Division of Child and Maternal Hygiene, Department of Pensions and National Health, and the closely allied subject of the treatment of live births under twenty-eight weeks' gestation was the subject of a report prepared and presented by the Vital Statistics Branch. In the first instance it was resolved in view of certain clinical and international considerations that the problem required further extended inquiry and study and that the Subcommittee on Stillbirth Registration and Certification of the Canadian Public Health Association be requested to continue their work in this field. In the second instance the present statistical practice of excluding from both the birth and death statistics events where death occurred within twenty-four hours should be revised to conform with Rule No. 19 laid down by the American Public Health Association according to which all infants born alive (in accordance with the accepted Canadian definition) shall be included in the birth and death statistics and be registered as such, regardless of the period of gestation.

The delegates felt that the production of current vital statistics data was most desirable. In view of the fact that the Dominion Bureau of Statistics contemplates planning with the provinces the issuance of a current Monthly Report on Vital Statistics for Canada, it was agreed that the Canadian Public Health Association be asked to set up a special committee under its Vital Statistics Section to study this problem with particular reference to present requirements in the health field, and to recommend the general scope of the public health material which should be incorporated in such a monthly report.

The procedure for the treatment of deaths occurring among the personnel of the Armed Forces of the Dominion was fully discussed, representatives of three branches of the Armed Forces and the Merchant Marine being present and contributing very materially to the deliberations. A distinct understanding was reached as to the course to be pursued. Dr. Paul Parrot, Demographer, Ministry of Health and Social Welfare, Quebec, presented a paper on the problems arising out of the registration of deaths of enlisted personnel.

The important question of the issuance of detailed vital statistics by place of residence was discussed at length. It was finally resolved that the Dominion Bureau of Statistics be requested to compile the national and provincial tabulations of vital statistics on the basis of residence, with

the exception of certain basic hospitalization tables by place of occurrence, commencing with those for 1943.

The problem of the form and content of both provincial and municipal annual reports was discussed and it was decided that this question should be referred to the Committee on Form and Content of the Annual Vital Statistics Reports of the Vital Statistics Section of the Canadian Public Health Association for consideration.

A valuable contribution was made by Dr. Enid Charles, Census Research Specialist, Dominion Bureau of Statistics, in the presentation of a paper regarding the desirability of developing a system of national divorce statistics. She demonstrated very clearly the social interest which would emanate from adequate divorce statistics and the national advantage of such statistics. The Bureau of Statistics was requested to canvass the field with the provincial and federal authorities concerned and prepare a draft form for consideration at a subsequent conference.

The question of the desirability of adoption statistics was ably presented to the conference by Dr. G. F. Davidson, Executive Director, Canadian Welfare Council, Ottawa, and it was decided that the Bureau prepare a draft report form along the lines advocated by Dr. Davidson with a view to introducing a national system of adoption statistics. It was further agreed that each province set up a routine procedure for the transmission of signed adoption orders or certified copies of adoption orders of children adopted within the province, but whose births occurred outside the province, to the Division of Vital Statistics of the province where the birth occurred. Any certificate of birth issued from such adoption orders or certified copies shall be issued in the adopted name of the child.

Another live problem was discussed; namely, the procedure followed by the provinces for delayed registration of births. This question involves what facts and what proofs are available or required in each province when registering a birth in later life. The constantly increasing demand for birth certificates due to the present war has made this a vital subject.

Several reports explaining the work done by the Bureau in issuing code books and manuals for the guidance and use of physicians, medical students, provincial registrars and others in the collection and teaching of vital statistics were submitted by the Vital Statistics Branch.

The conference recognized the value of the Vital Statistics Section of the Canadian Public Health Association as a clearing-house for the study and discussion of technical health problems in vital statistics, and urged that the activities of that section be continued and extended in order that subsequent conferences of this type might benefit by such studies as might be undertaken by it.

The conference recorded its appreciation of the constant co-operation given by the medical profession in reporting births and in certifying deaths and would welcome any suggestions the profession might make toward the improvement of vital statistical practices or of the statistical data which are presently compiled. Therefore, the conference undertook to collaborate closely with the Canadian Medical Association, through its delegate, in the solution of such pertinent mutual problems as might arise from time to time.

It was agreed by all present that free interchange of ideas and discussion of public health problems were essential in improving the vital statistics of Canada and achieving quickly a solution of problems as they arose. It was, therefore, urged that a Dominion-Provincial Conference should be held every year and at a time when attendance on the part of the members of the Dominion Council of Health would be possible. It was resolved that this request be conveyed to the Honourable the Minister of Trade and Commerce for his consideration.—E. CLARKE, *Statistician, Dominion Bureau of Statistics, Ottawa.*